BRAIN.

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Original Articles and Clinical Cases.

SOME OBSERVATIONS ON PRIMARY DEGENERATION OF THE MOTOR TRACT.

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CASE No. 1.

A case of *amyotrophic lateral sclerosis* of fifteen months' duration. General muscular wasting beginning and more pronounced in arms and hands. Exaggerated reflexes. Loss of sphincter control. Later pronounced bulbar symptoms. Extreme general wasting and great helplessness. No sensory symptoms. *Microscopically.*—Degeneration of large cells of motor cortex and of efferent tract through capsule, pons, medulla, and spinal cord, also in fibres of corpus callosum. Tangential, super- and interradial cortical fibres not affected. In the medulla atrophy of cells of ninth, tenth, eleventh, and twelfth nuclei. In the cord atrophy of anterior horn cells

in lateral and postero-external groups of cervical and lumbar regions. Degeneration of fibres in anterior commissure and in antero-lateral ground bundles. No change in posterior columns. Atrophy of peripheral nerves and of muscles. Vessels in a condition of slight arterio-capillary-fibrosis.

Clinical History.[1]

E. H., female, aged 33. Admitted to Claybury Asylum for general paralysis, November 11, 1895. Unmarried; occupation, general servant. She says that up to a year ago she had been able to do her work quite well. She then noticed that her hands became weak. Although her speech is thick and indistinct, she gives perfectly rational answers to questions. Her memory, she says, is not so good as it was, and she and her friends have noticed a progressive defect in her speech. She has a small head and large projecting chin, and this, taken with her lachrymose condition, gives her an imbecile appearance, although, on conversation with her, it is apparent that she cries because of her helpless condition. The pupils are equal and react to light and to accommodation. There is a marked wasting of the muscles of the hand and forearm, with a condition of *main en griffe*, rendering her quite helpless. The thenar and hypothenar eminences are particularly wasted; also the interossei. She is unable to extend the fingers. The muscles of the body are generally wasted, but the shoulder muscles not in particular. The respiratory movements are mostly diaphragmatic, the upper part of the chest moving very little. There is a general wasting of the muscles of the leg, and a tendency to foot-drop and inversion. There is very marked foot-clonus, patellar clonus, and wrist-tap contraction obtainable. She has lost power over her sphincters, and she has some difficulty in swallowing and masticating her food. She protrudes the tongue with difficulty when asked, and she cannot protrude it far beyond the teeth; it is tremulous. There is no loss of sensibility. The muscles were tested with the faradic current, and responded; but a stronger current than usual was required. A systematic examination was impossible, owing to the patient's lamentation.

November 26.—Patient is much weaker; bulbar symptoms much more manifest, both in difficulty of speech and swallowing. She is very emotional, and continually cries out for water. She still goes about the ward wheeled in a chair. The left pupil is

[1] Reprinted from *The Archives of Neurology*, Vol. I., p. 359.

rather larger than the right, but they react to light and accommodation. Her craving for water is no doubt due to polyuria, for she is always wet.

January 29, 1896.—Patient is much feebler and more helpless, muscular wasting more marked. Knee-jerks and wrist-tap contraction very exaggerated. Can feel the lightest tactile sensation on the leg; can protrude the tongue between the teeth, but the speech is much more muttering and indistinct, although she seems to know what she wants. She is now unable to swallow even minced food. She passes a large quantity of water under her, which cannot therefore be measured. She continually asks for water. Her extremities are cold, and she is evidently sinking fast. A few days later she was affected with ulcerative colitis from which she died.—F. W. Mott.

Autopsy and Notes by Dr. Stansfield, February 13, 1896.

Muscles wasted; skull symmetrical, thick; dura mater slightly thickened; pia-arachnoid somewhat opaque and thickened; Pacchionian bodies numerous at vertex along mesial line; convolutions large, simple; sulci shallow; cortex small in amount, fair consistence, pink, striation marked; ependyma smooth. *Cord.*—Recent hæmorrhage round the dura in cervical region, the clot being dark and soft, extending from 4th cervical to 5th dorsal; cord soft, flabby, wasted in the cervical and upper dorsal portions. In the region of the lumbar enlargement it is much firmer, and there is no apparent wasting. Muscular tissue of heart very soft, brown, and small in amount; weight, 5 oz. *Liver.*—39 oz.; slightly fatty. *Spleen.*—4 oz.; firm. *Kidneys.*—9½ oz.; capsule slightly adherent. Large intestine congested throughout its entire length. Two ulcers in the first part of rectum, one large, about ¾ in. in diameter, with thick, overhanging margins.

Cause of Death.—Ulcerative colitis and dementia of general paralysis. (Microscopic examination and the smooth ependyma of the ventricles showed that this was not a case of general paralysis.—F. W. Mott.)

Microscopical Examination.

Brain.—The large pyramidal cells of the third layer are diminished in number, and many of those which are present show important pathological changes. Many of them have quite lost their normal shape, and are swollen and globular looking; others are shrunken and atrophied. In many

instances the nucleus and cell processes are very indistinct; most of the cells also contain a large amount of yellow granular pigment. These degenerative changes are confined to the large cells, the small and medium-sized pyramids being quite healthy. Throughout all the cortical layers small round cells and Deiters' cells are present in large numbers, but especially so in the deepest polymorphic and granule layers. An examination of Marchi-stained sections shows that there are large numbers of degenerated fibres throughout the white substance, and also in the corpus callosum, most of such fibres being of large size.

The tangential, super- and interradial systems of fibres are well seen, and show no change; indeed, a particularly abundant layer of tangential fibres is present.

The pia-arachnoid is thickened in places, and its vessels are distended. Fatty changes are also present in many of the capillaries of the brain, but such do not bear any relation to the areas of cellular degeneration.

Internal capsule.—There are many fibres undergoing recent degeneration, but carmine and Weigert preparations do not reveal any definite area of sclerosis.

Crura.—Many fibres undergoing degeneration occur in all parts of the pes, and at this level definite interstitial sclerosis can for the first time be made out, especially in the mesial portion.

Pons and Medulla.—Recent degeneration, with slight interstitial overgrowth, occurs throughout the efferent tract. There are also well-marked degenerative changes in the cells of the ninth, tenth, eleventh and twelfth cranial nerve nuclei.

Spinal cord.—Cervical enlargement (C. 2, 3, 4, 5, 6, 7, and 8, D. 1 and 2). At all these levels there is recent (Marchi) degeneration with interstitial sclerosis in the crossed pyramidal tracts. Some slight sclerosis exists in the direct tract, which, however, cannot be traced lower than the second dorsal segment. There is also a little degeneration in the lateral ground bundles, which is probably due to the involvement of commissural fibres; also a few degenerated fibres in the anterior commissure. No other portions of the white matter are affected.

The anterior horn cells are much diminished in number,

and most of those which remain are undergoing degeneration. These changes do not affect all the cell groups however; the mesial-anterior group is practically normal, and the change is most marked in the lateral and postero-external groups; within these groups there are scarcely any large ganglion cells having a healthy appearance. The condition appears to be one of chronic atrophy, there being no evidence of acute change. The cell gradually becomes smaller and withered-looking; it loses its characteristic multipolar shape, and is fusiform or crescent-shaped. The chromatic substance loses that regular arrangement which is such a pronounced feature of a healthy anterior horn cell; occasionally it has completely disappeared, its place being taken by a mass of yellow pigment, which stains black with Marchi fluid. The nucleus is frequently eccentric, the nuclear membrane very ill-defined. The cell processes are fewer in number, and often broken off short, and the anterior roots are atrophied. The posterior roots show no change.

In addition to these alterations in the cells there is a very great decrease in the number of fibres composing the network of the anterior horns; such diminution is especially marked in the more central parts of the horn.

Dorsal region (D. 3, 5, and 8).—There is well-marked interstitial sclerosis in the crossed pyramidal tracts in all these segments, but the amount of recent (Marchi) degeneration is very much less than in the cervical region. Recent degeneration and sclerosis also exist in the anterior commissure to a slight extent.

The anterior horns are practically normal, it being impossible to make out any diminution in the number of cells or fibres composing them, neither can any degenerative changes be seen. The cells of Clarke's column are likewise healthy, and not decreased in number.

Lumbar region (L. 3 and 5).—The crossed pyramidal tracts show precisely similar changes to those in the higher parts of the cord, except that there is more interstitial sclerosis and less recent degeneration. There is, however, plenty of recent change in the antero-lateral columns, and also in the anterior commissure.

Alteration in the structure and decrease in the number of the anterior horn cells exist as in the cervical region, but to a far smaller extent; such changes being also most pronounced in the lateral and postero-external cell groups.

Membranes.—There is a slight thickening of the pia-arachnoid all round the cord, which is greatest on the anterior surface. The walls of many of the small and medium-sized *vessels* are slightly thickened and fibrous; the *central canal* is normal throughout.

Ulnar nerves.—Transverse sections of hæmatoxylin preparations show that in each bundle there are many fibres which remain unstained. There is also a slight increase of fibrous tissue, but Marchi sections show comparatively little recent degeneration.

Thumb muscles.—Many of the fibres have completely lost their striation, some being clear and homogeneous looking, others finely granular, and others in a condition of actual disintegration. Marchi-stained sections show that throughout the entire muscle there are many fibres in a state of fatty degeneration; in between those undergoing the above changes, however, fibres occur which appear to be perfectly healthy.

Case No. 2.

A case of *amyotrophic lateral sclerosis* of eleven months' duration, beginning with painful cramps, followed by loss of power in right leg. Left leg, right arm, and left arm shortly afterwards affected. General muscular wasting, most pronounced in small muscles of hands. Exaggerated reflexes. Later, loss of control over sphincters. Delirium, extreme helplessness. No impairment of sensation. Pronounced bulbar symptoms shortly before death. *Microscopically.*—Recent degeneration of projection fibres in motor area of brain, also in corpus callosum, but no alteration in cells. At level of pons sclerosis begins in pyramidal tracts and continues to the furthest extent of the cord. Cells of anterior horns atrophied in C. and L. regions, also decrease in network of anterior horns. Glossopharyngeal and hypoglossal nuclei affected. Clarke's column normal. Sclerosis

in Goll's and antero-lateral columns. Universal arterio-capillary-fibrosis. Atrophy of fibres of peripheral nerves.

Clinical History.

J. G., male, aged 67 ; occupation, labourer ; was admitted into Charing Cross Hospital under Dr. Mott, on January 3, 1898, for muscular weakness. There is nothing in the family history bearing upon the case. The patient has been a soldier, and served through the Crimean War and the Mutiny. Whilst in India he had dysentery, and also a chancre and bubo. His present illness began four and a half months before admission; he had previously been working in a white lead factory for three weeks. He first noticed a painful cramp in the right knee, which persisted and became so bad that in a month's time he was unable to walk. He then began to lose the power of movement in his right leg, and had periodic attacks of twitching and cramp in this limb; according to the patient such attacks lasted from ten to thirty minutes ; he described the limb as being "all of a shake," and states that if he were standing when such an attack came on he would fall down. The left leg then became similarly affected to the right, but there was less pain ; finally he lost all power of standing. Shortly after this he noticed loss of power in the right arm, and a little later the same in the left. He has suffered with constipation since the illness commenced.

On admission.—Patient is fairly well nourished, he sits propped up in bed in great distress during the periodic attacks of pain; he sweats profusely at times; complains of a disagreeable smell in the nostrils. He answers questions rationally, but is very emotional, bursting into tears when narrating his illness. He passes a normal quantity of water with a trace of albumen. His appetite is good; he complains of thirst. *Heart.*—Sounds muffled, but no murmur. *Lungs.*—Emphysematous. *Abdominal viscera.*—Nothing abnormal detected. *Nervous system.*—The patient has not sufficient power to raise or lower himself in bed, and is quite unable to stand alone. The muscles of the arms and legs generally are much wasted, but particularly the interossei and those of the thenar and hypothenar eminences of the right hand. He has great difficulty in flexing the knee joints, but can flex and extend his toes and also perform external and internal rotation of his feet. Fibrillary twitchings can be seen in the muscles of both legs and of the right arm. The deep reflexes are markedly exaggerated, knee-jerks being excessive, ankle clonus present, and wrist-tap contractions readily obtained. There is no

loss or impairment of sensation to touch, heat and cold, or pain. Sense of position is likewise unimpaired. Smell, sight, hearing, and taste good and no difficulty in swallowing or talking.

January 17.—The patient now suffers considerably less pain; when present it begins at the ankle and stops at the knee, seldom reaching as high as the groin. His arms seem weaker, and he complains of being very thirsty.

February 3.—Still pains of a shooting character in the legs, right more than left. He also has pain in the right wrist and metacarpo-phalangeal joints, and the hand is slightly œdematous.

Electrical examination.—Right arm. With the faradic current, the deltoid does not respond, the interossei and the extensors of the fingers respond only sluggishly to a fairly strong current. With the galvanic current, the deltoid and extensors react normally, but require a moderately strong current; the interossei react to K.C.C., but a stronger current than normal is required. There is no reaction of degeneration.

Left arm.—With the faradic current, the interossei respond if a strong current is used; all the other muscles of the arm and forearm respond to a slightly increased current. With the galvanic current all the muscles react normally.

Legs.—With the faradic current, none of the muscles of either leg react. With the galvanic current, there is a sluggish response in all the groups, if a strong K.C.C. is used.

March 5.—Patient began to lose control over his sphincters.

March 4.—Delirious in the night.

March 14.—Complained of severe pains in the lower part of spine, for which morphia had to be given hypodermically; this pain persisted, and was so severe that the injections had to be continued constantly.

He remained in this condition for some months, then his articulation became so affected that it was impossible to understand him. A few days after the onset of this symptom he began to have difficulty in swallowing; even fluids at times caused him to choke, but they did not return through the nose. He was very emotional. Shortly afterwards, a pressure sore appeared on the inner side of each knee. He was always very thirsty, and gradually became weaker till his death on July 15, 1898, about seven months after admission.

The affection of the muscles was such that for some months before he died he was quite unable to move his arms to feed himself; their position was adduction at shoulder, flexion at elbow, and flexion of the thumbs and fingers; this position persisted until

death. Six weeks before he died, right foot-drop was very marked, and both feet were œdematous, and the ankles very painful. Latterly he knew when he passed his water, but it was all passed under him. He never had any squint or affection of sight. He always complained of thirst. The temperature was normal throughout his illness, till three or four days before death.

Post-mortem Notes.

Body wasted. P.M. staining slight, and at most dependent parts only; rigidity passing off; no bed-sores.

Thorax.—Rib cartilages ossified; both lungs œdematus and deeply pigmented; emphysema along borders. Pericardium contains half an ounce of clear fluid; the membrane has several opaque patches. The heart weighs 9 oz.; muscle is normal, and the valves competent. There is extensive atheroma of the first part of the aortic arch.

Abdomen.—Mucous membrane of the stomach is atrophied. The liver is fatty and congested, and weighs 2lbs. 5oz. Gall bladder and its ducts are normal. The spleen is adherent and friable. Kidneys.—Left weighs 7½ oz., capsule is adherent, and the whole organ congested; right weighs 3 oz., and contains numerous cysts, which are filled with fragments of calcareous matter; the pyramids are wasted, and the pelvis inflamed. Bladder is small, and its mucous membrane in a condition of chronic inflammation. Pancreas is normal.

Brain.—The dura is normal; and the Pacchionian bodies are large and prominent. The sulci in the central regions are filled with opaque lymph, and the pia-arachnoid is opaque and somewhat thickened.

Microscopical Examination.

Brain.—Sections of the motor region stained by Marchi's method reveal the presence of many degenerated fibres of the projection system, many such are also found in the corpus callosum. Unfortunately the method by which the brain had been hardened made it impossible to use Nissl's stain, but in sections stained by the carmine and Weigert-iron methods there does not appear to be any alteration in the cells. The tangential and supraradial fibres are likewise normal. The pia-arachnoid is considerably thickened in places, and there is also fibrosis of the middle and outer

coats of many of the small and medium-sized arteries; in many of the vessels this thickening is of a hyaline nature, but there is no endarteritis.

In the *crura* and upper part of the *pons* there is abundant recent degeneration without sclerosis of the fibres of the efferent tract; in the lower part of the pons the presence of an interstitial sclerosis becomes evident, and from thence continues downwards as far as the sacral region of the cord.

In the *medulla* there is very marked diminution in the number of cells lying around the floor of the fourth ventricle. The nuclei of the ninth and tenth cranial nerves are particularly affected; not only are there very few cells, but nearly all those which are present are in a condition of advanced degeneration, almost exactly the same as the anterior horn cells presently to be described. The nucleus of the twelfth nerve is also affected, but to a somewhat less extent.

Spinal cord.—Cervical enlargement (segments C. 2, 3, 4, 5, 6, 7, 8; D. 1 and 2). In all these sections there is very considerable recent degeneration with interstitial sclerosis in both crossed and direct pyramidal tracts; one of the latter is more affected than the other, which is evidently due to the direct tracts being unequal on the two sides, as not uncommonly happens. Within the affected areas there is a great diminution in the number of fibres, and the majority of those which remain are of small calibre, which apparently shows that the large fibres are those chiefly affected. In the lateral columns the degenerated area exactly corresponds with that of the crossed pyramidal tract, and the zone of white matter intervening between the inner border of this and the gray matter of the horn (lateral limiting layer) is perfectly healthy. There is also a similar degeneration and sclerosis in the antero-lateral columns in the form of a narrow band extending from nearly as far forwards as the direct tract to nearly as far backwards as the crossed, and lying midway between the gray matter and the periphery of the cord (fig. 2, Plate I.). This is probably partly due to degeneration of commisural fibres connecting the upper and lower limbs, as it can be

traced as far down the cord as the lumbar enlargement; possibly in the cervical region it is also partly due to the atrophy of outgoing fibres from the anterior horns, as the anterior roots are noticeably affected. Recent degeneration and slight sclerosis are also present in the posterior columns, corresponding to an early tabetic lesion affecting the root zone in the lumbar region and Goll's column above.

In addition to these changes in the white matter there is a very marked diminution in the number of the anterior horn cells. This change is practically confined to the lateral and postero-external cell groups, the mesial-anterior group showing scarcely any change. Within the affected groups nearly all the cells which remain are in a condition of chronic degeneration, and of many of them all that remains is a small collection of granular pigment. The network of fibres in the middle portion of the horn as well as in the posterior commissure is also exceedingly scanty, owing to the atrophy and disappearance of a large number. Carmine-stained sections show the presence of numerous Deiters' cells and sclerotic tissue in these regions. These changes in the anterior horn cells are much more marked in the lower cervical and first two dorsal segments than they are in the higher part of the cord, that is, in that portion of the cord from whence arise the nerves supplying the arm and hand. In this region the atrophy of the anterior horns is so pronounced that it is quite evident to the naked eye.

The anterior roots are small and contain many atrophied fibres, but show very little recent degeneration.

Dorsal region (Segments 5, 6, 8, 10, and 12).—The change in the direct tract becomes much less marked at the level of the eighth segment, otherwise the recent degeneration and sclerosis in the efferent tracts is similar to that in the cervical region; the lateral limiting layer being also quite unaffected. The change in the antero-lateral columns is likewise similar in nature and situation, but in the posterior columns at the level of the tenth and twelfth segments, although the sclerosis is best marked in the inner portion of Goll's column, there is a slight interstitial increase throughout both postero-internal and external tracts.

It is quite different, however, with the anterior horns. Throughout the whole of the dorsal region these cells appear quite healthy, and are not noticeably diminished in number, neither is there any decrease in the meshwork of fibres. There is no change in the cells of Clarke's column.

Lumbar enlargement.—In these segments sclerosis is still present in the lateral columns as a very well-defined triangular area. There is also slight sclerosis in the antero-lateral columns, and a diffuse sclerosis with diminution in the number of fibres throughout the posterior columns; in the latter region it is most pronounced in Charcot's root zone and the immediate neighbourhood of the posterior longitudinal fissure, except the small oval area of Flechsig.

The anterior horn cells are affected to an even greater degree than in the cervical enlargement, and all the cell groups to an equal extent. Not only are there comparatively few cells present, but those which remain are so profoundly altered that it is with great difficulty one can find any normal cells. Of those present many are little more than globular masses of yellow granular pigment, surrounded by a clear space, and apparently quite destitute of nucleus or processes. In others the change is not quite so advanced, and although the cell is very much shrunken and its outline altered, an indistinct nucleus and short, broken-off processes can still be recognised. In the anterior horn cells throughout the cord there is a very considerable deposit of granules of yellow pigment. In no instance could we discover any indication of acute changes in the cells.

Unfortunately the spinal ganglia were not preserved, but *no change* could be seen in the posterior roots.

Vessels.—Practically all the vessels of the spinal cord and also many of the smaller ones in the membranes are much thickened; this thickening involves the middle and outer coats; in some vessels it is fibrous and in others hyaline in nature. To many of the vessels there are well-marked processes of fibrous tissue radiating outwards from the adventitia, and insinuating themselves between the nerve-fibres. The intima appears perfectly normal, and we could find no trace of hæmorrhage, embolus, or throm-

bus. This condition of arterio-sclerosis is similar to that described by Gull and Sutton; its presence was also noted in the brain, indeed, it is universal throughout the nervous system, although most marked in the cord.

Membranes.—In the brain there is very marked thickening of the pia-arachnoid over the motor convolutions. In the cord this membrane is also greatly thickened, but only on the anterior and lateral surfaces, no change being evident in the membrane over the posterior columns. The septa passing into the cord from the periphery are also very much thickened.

Ulnar nerves.—There is a very marked diminution in the number of nerve-fibres in all the fasciculi, their place being taken by an increase of fibrous tissue. This condition is seen in transverse and longitudinal sections. Marchi-stained sections do not show any recent degeneration.

Case No. 3.

A case of *progressive muscular atrophy* of over four years' duration; beginning with weakness in right arm, and a few months afterwards in left arm. Weakness and wasting of various muscles of arms and shoulders, with absent reflexes. Knee-jerks exaggerated. Speech and swallowing not affected. Admitted into hospital for severe cystitis, of which he died within ten days. *Post mortem.*—Chronic cystitis with early suppurative nephritis. Extreme degeneration of anterior horn cells in cervical enlargement, antero-internal group least affected, atrophy of anterior roots. No change in anterior horns in D. and L. regions. Slight sclerosis in posterior columns; slight sclerosis in crossed pyramidal tracts in lumbo-sacral region, no change in pyramidal tract above. Universal arterio-capillary-fibrosis.

Clinical History.

E. S., male, aged 57; cabman; was admitted into Charing Cross Hospital, under Dr. Mott, on July 14, 1896, suffering from retention of urine.

There was nothing in the family history bearing upon the case.

The present illness began a little over four years ago with

weakness and wasting in the right hand. Later, in March, 1892, he was lifting a box on to his cab when he fell backwards, and the box fell on him. He was unconscious for a few minutes, but soon recovered, and then drove his cab to the station. The same day the weakness in the right arm became worse, and about three months afterwards he began to experience loss of power in the left arm. Since June, 1892, the patient has been unable to use his right arm for driving, and since October, 1892, the left arm has been useless for the same purpose.

This helpless condition of the patient led to him going the whole day without passing water, as he found difficulty in using either hand. For the last seven or eight months, however, his urine has constantly dribbled away, which he thought was due to weakness. This condition not getting better, the patient came to the hospital; it was then found that he had retention with overflow.

On making an examination of the patient, he was found to have marked progressive muscular atrophy, although he probably would not have presented himself for treatment had it not been for the bladder trouble.

At first sight it might appear that the onset of the muscular atrophy was due to the accident in March, 1892, but the patient is quite definite that he had noticed some weakness and wasting in the right hand for a short time before this. This being so, the accident was probably the effect and not the cause of the disease; further, the subsequent *gradual* progress of the wasting, and the fact that it was three months before the left hand became affected, is against the view that the disease was the result of hæmorrhage into the gray matter of the cord.

On admission.—Power of movement. In the right arm slight flexion and extension of the fingers can be performed, but not of the thumb. Extension of the wrist is entirely absent, but some power of flexion remains. Pronation and supination are absent. There is no power of flexion at the elbow, but some power of extension. At the shoulder joint abduction and adduction are wanting; slight rotation is possible; elevation is practically normal. Left arm.—Movements of the fingers and wrist are the same as in the right arm, but slightly stronger. Pronation and supination are absent. Flexion and extension of the elbow joint can be performed fairly well, and the hand can be brought nearly up to the mouth. Abduction of the arm at the shoulder can be performed; there is fair antero-posterior movement, and some rotation. In the lower limbs movements at all the joints appear normal.

Nutrition.—The interossei and the thenar muscles of both hands are much wasted, as are also the muscles of both forearms. On the left the supinator longus is well preserved. The biceps is practically gone on the right, and much wasted on the left. The triceps are still fairly preserved on both sides. Both deltoids are atrophied; the pectorals, trapezei and the serrati magni are fairly strong. There is some wasting of the muscles of the neck. The skin over the fingers of both hands is red and sticky. The right wrist joint is very lax, and allows of extension and passive movement; there is fulness over the synovial sheaths of the flexor tendons. There is some grating in the right shoulder joint on passive movement. Fibrillary twitching is observable in the muscles of the right forearm. The muscles of the legs generally are slightly wasted, but no group is especially affected.

Sensation.—Tactile sensation is slightly impaired in both legs, and in the right hand, especially over the ring finger.

Reflexes.—These cannot be obtained in either arm; in the legs the knee-jerks are very brisk, but there is no clonus.

Electrical reactions.—The reactions of the muscles of both upper extremities are diminished quantitatively. In the muscles of the thenar eminence of the right hand all reactions seem to have disappeared. All the muscles show polar changes, A.C.C. being distinctly greater than K.C.C. The contractions, however, are not sluggish. Stimulation of the muscles through the nerve trunks by galvanism or faradism produces contractions. To the faradic current the reactions of the muscles are normal, prompt contractions being produced by a moderate strength of current. Sensibility to both currents seems about normal.

Speech is unimpaired. *Deglutition* is normal.

Urine is very pale and opalescent; sp. gr. 10·10; alkaline in reaction; contains pus and albumen in considerable quantity.

July 22.—There is no change in the nervous or muscular symptoms, but patient says that he feels very weak, and he is evidently very ill. His pulse is 120; he has had persistent hiccough for the last two days; complains a good deal of pain in the umbilical region, and, in spite of energetic treatment, the cystitis still persists.

July 24.—Patient is so ill and exhausted that he speaks with difficulty. Pulse 66, very irregular and collapsing. Early this morning he had an attack of syncope, but came round on the administration of strychnine and ether. Pupils are rather irregular, the left being more contracted than the right.

He gradually sank and died the same evening, there being no alteration in his nervous symptoms.

Post-mortem Notes.

All the organs were found to be healthy, with the exception of the genito-urinary apparatus. There was well-marked chronic cystitis, the mucous membrane of the bladder being much thickened, and covered with phosphatic deposit; here and there were areas of acute inflammation; there was commencing suppurative nephritis.

Brain.—The pia-arachnoid was slightly opaque and thickened over the central convolutions. Here and there were a few small cysts, varying in size from that of a hemp to a millet seed. These might probably be due to early decomposition, or be small softenings resulting from vascular change. The ventricles were not granular, and the membranes were not adherent.

Spinal cord.—The dura mater showed no naked-eye change. The whole of the lower cervical and upper dorsal regions of the cord were remarkably flattened, and on section there was obvious atrophy of the anterior horns. The lower dorsal and lumbo-sacral portions of the cord seemed perfectly normal.

Microscopical Examination.

Unfortunately the ganglion cells of the motor cortex could not be examined by Nissl's method, but in sections of the crura, pons, and various levels of the medulla the efferent tracts are perfectly normal; indeed, the sections of the central nervous system above the level of the cord show no pathological change, with the exception of some thickening of the middle and outer coats of the smaller vessels.

Spinal Cord. Cervical Enlargement.—(C. 4, 5, 6, 7, and 8). In all these sections the cord is flattened and wasted, and the anterior horns are obviously abnormal in shape and much atrophied. Throughout the whole of the enlargement there is pronounced diminution in the number of the anterior horn cells, and those which are present are in an advanced condition of degeneration, it being almost impossible to find a healthy cell in this region. The change undergone by these cells is a chronic one, associated with the deposition of much granular pigment, precisely the same as that described in the other cases; the mesial-anterior group of cells in this case also being less affected than the other cell nests.

There is also a very noticeable decrease in the network of fibres of the central portion of the horns, the fibres lying towards the periphery not being nearly so much affected; in the middle of the horns considerable numbers of Deiters' cells are also present.

At the level of the sixth segment in one of the horns there is a small focus of softening containing altered blood corpuscles and granular masses of pigment.

The anterior roots arising from this region are small, and many of the fibres are seen to be atrophied.

There is definite interstitial sclerosis at the periphery of the cord in the antero-lateral columns, with some thickening of the adjacent pia-arachnoid membrane. Probably this peripheral sclerosis is due to the atrophy of outgoing motor fibres, rather than to the involvement of one of the tracts of the cord. The change ceases above the fourth cervical, and below the second dorsal segments; its situation also exactly coincides with the area of emergence of the anterior roots. The thickening of the investing membrane and of the septa in this region is probably also the result of irritation by products of degeneration carried outwards along the nerve roots. Slight interstitial sclerosis is also present in the intermediate portion of the antero-lateral columns; this is no doubt due to atrophy of association fibres.

Dorsal Region. (D. 3, 6, and 8.)—In these sections the anterior horns are perfectly normal, both with regard to cells and fibres. The anterior roots are also healthy. The cells and the reticulum of Clarke's column are abundant, and show no change.

Lumbar Enlargement. (L. 4 and 5; Sa. 1.)—In none of these sections is there any change whatever in the cells or fibres of the anterior horns. Marchi sections show a few black dots amongst the fibres of the anterior commissure and in the posterior columns there is slight interstitial sclerosis, indeed, both postero-external columns in all regions of the spinal cord contain many fibres undergoing degeneration, with some interstitial sclerosis, as shown in fig. 3, Plate II. Many of these from their situation are undoubtedly endogenous association fibres, and due to destruction or

degeneration of cordonal cells at the base of the posterior horn in the atrophied portion of the cord.

In all these sections through the lumbar region there is definite interstitial sclerosis with atrophy of nerve-fibres in the crossed pyramidal tracts of both sides; it is most marked in the fibres lying nearest the surface of the cord, which are probably the longest fibres in the upper efferent tract. This is of interest as showing the primary degeneration of the terminal branches of the cortical pyramidal neurones with the longest axons, and accords with the brisk knee-jerks.

Vessels.—Most of the vessels throughout the cord are in a condition similar to that described by Gull and Sutton (arterio-capillary-fibrosis), the media and adventitia being much thickened, at times fibrous, at others hyaline in appearance. Surrounding many of the vessels there is quite a thick overgrowth of fibrous tissue which extends in a stellate manner into the adjoining nervous tissue.

A medium-sized vessel on the anterior surface of the cord in the lumbar region shows pronounced thickening of the intima (*endarteritis obliterans*), but this is the only vessel showing such change which was discoverable amongst all the sections examined.

Membranes.—The pia-arachnoid is slightly thickened throughout the whole extent of the cord, but most on the anterior and lateral aspects. In the cervical region products of degeneration (myelin and fat-globules of varying sizes, and fat-carrying leucocytes) occur in considerable quantity between the membranes and the external surface of the cord.

Posterior Roots.—Many of the incoming fibres of the posterior roots in all the regions examined are degenerated; unfortunately the ganglia were not removed, so that it is impossible to say what was the condition of these.

Case No. 4.

A case of *chronic rheumatoid arthritis with muscular atrophy* of several years' duration, beginning with pains in feet and afterwards in hands, followed by contractures. Pronounced deformities of all limb joints, especially the

smaller ones, with osteophytic outgrowths and considerable muscular wasting. Sensation, speech, and swallowing normal. Death from broncho-pneumonia. *Microscopical examination.*—No change in either white or gray matter of brain, pons, or medulla. In the spinal cord chronic atrophy with excessive pigmentation of anterior horn cells in cervical and lumbar enlargements, all groups affected (especially the mesial-anterior). Decrease in fibrillary network. General slight interstitial overgrowth throughout the cord with arterio-capillary-fibrosis, but no tract degeneration; slight chronic changes in cells of posterior ganglia, atrophy of peripheral nerve-fibres, atrophy and fatty degeneration of muscles.

Clinical History.

J. D., aged 53, widow; charwoman; was admitted into Colney Hatch, February 15, 1896. Medical certificate on admission:—She is dull and depressed, she talks incoherently, and declares that other patients are spreading a number of bad reports about her, and that she can hear voices outside the ward and up in the ceiling. She thinks she is to marry the doctor, and that several children are in the ward.

She gives the following *history* of herself:—Four years ago she had pains in the feet, and then in the knees, which subsequently became contracted, preventing her walking. Two and a half years ago the hands also became affected with pains, afterwards followed by considerable rigidity of the elbow and hand.

Her *present condition* is as follows:—She lies in bed on her right side, with her chin resting on the sternum, the movement of the head being very limited.

Lower limbs.—The hips are flexed on the body, the knees are flexed, and the ankles extended. The end of the femur can be seen projecting in front of the head of the tibia, the internal condyle is prominent, the patella is thrown outwards, resting on the outer condyle; the head of the fibula projects externally; there are considerable numbers of osteophytes developed; the knee-joints are apparently ankylosed; the internal and external malleoli are prominent, and the ankle-joint is fixed; the big toe is turned outwards, but does not cover the digits. The four digits are over-extended at the metatarso-phalangeal joints, and fixed at the first interphalangeal joint, where there is considerable thickening. There is pronounced muscular wasting of the limbs.

Upper limbs.—Here the most marked deformities are in the

hands. There is flexion of the ungual phalanx on the second to an obtuse angle, extension of the second phalanx on the first, and flexion of the first phalanx on the metacarpal bone; flexion to a less obtuse angle of the metacarpus and carpus on the bones of the forearm. There is ulnar deviation of the hand, and a prominence of the first metacarpo-phalangeal joint. The forearm is pronated, and the elbow flexed. The shoulder joint is rigid, and the upper limb is fixed to the chest in a position of adduction. The finger-nails are small and atrophied.

There is great nodular deformity about the metacarpo-phalangeal joints and the wrist, and all the muscles are much wasted. The skin of the hands is smooth, red, and cold, and has lost its wrinkles, but there is no loss of sensation.

The muscles most wasted are the small muscles of the hand, forearm, arm, foot, leg and thigh, in the order mentioned. All these respond readily to faradism. K.C.C. is less than A.C.C. There is no fibrillary twitching.

There is no loss of sensation, and no loss of control over the sphincters. The diaphragm during respiration contracts rather more forcibly than is usual in a woman. There is no affection of speech or of swallowing. (F. W. M.)

No change occurred in her mental and physical condition, and three months later she died of broncho-pneumonia.

Post-mortem Examination.

It was found to be quite impossible to move the joints out of the abnormal positions which have been described. There were no bedsores.

The brain appeared fairly normal, and sections showed no naked-eye change; several portions were preserved for microscopical examination. The membranes were not thickened, nor were they adherent.

The spinal cord showed no naked-eye change; it was preserved with several of the spinal ganglia for further examination.

Heart.—Small, weighing only 6 oz. No valvular lesion, muscle substance of a dark reddish colour, contrasting in this respect with the atrophied skeletal muscles.

Lungs.—Pneumonia and recent pleurisy of the right upper lobe. *Liver.*—Very large, 64 oz., nutmeg appearance on section, did not give the iron reaction. *Kidneys.*—6½ oz. the pair, very pale and obviously fatty, especially the cortex. *Spleen.*—4 oz., pale and somewhat diffluent.

The atrophied limb-muscles were very pale, and appeared to be infiltrated with fat.

Microscopical Examination.

Brain.—Motor cortex. Sections stained by Nissl's method show no pathological change whatever in the cortical cells. The vessels are healthy, and there is no thickening of the membranes.

The *internal capsule, crura, pons, and medulla* likewise appear perfectly normal.

Spinal cord.—Sections were examined at the level of the sixth, seventh, and eighth cervical; first, tenth, twelfth dorsal; second and fifth lumbar, and first sacral segments.

Gray matter.—In the cervical enlargement there are very important alterations in the large cells of the anterior horns. There are fewer such cells present than in the normal cord in this region, and a large number of them are seen to be undergoing a chronic degenerative change, with the deposition of a large amount of pigment, just like the change occurring in Cases No. 1, 2, and 3. In the present case, however, it does not appear to be quite so extensive, and there are some fairly healthy cells scattered amongst the atrophied ones; the process also does not pick out any special group of cells as in the other cases, but affects apparently to an equal extent all the different groups.

In the dorsal segments examined there is not anything like the same amount of change in the anterior horn cells; here and there degenerated cells occur, but they are comparatively rare, whereas in the cervical and lumbar parts of the cord the reverse is the case, and healthy cells are in a decided minority.

In the lumbo-sacral portion of the cord exactly similar changes occur as in the cervical enlargement, that is, many cells in various stages of degeneration are scattered throughout all the cell nests.

The mesial-anterior group certainly appears to be as much, if not more affected than any other, unless it be the postero-external. It has been pointed out that in the other cases this group shows practically no change.

In the cervical and lumbar enlargements there is also very considerable decrease in the fibres composing the network of the anterior horns, especially in the central portion. This change, which does not occur in the dorsal region, causes a very obvious pallor of the sections stained by Weigert's method.

The posterior horns, the cells and reticulum of Clarke's column, and the other portions of the gray matter, appear perfectly normal in all regions of the cord.

White matter.—In all the sections examined there is a slight general increase of the interstitial tissue; this is greatest towards the periphery of the cord, and in the neighbourhood of large fissures and vessels; the adventitia of the latter is also very much increased. In no instance do the nerve-fibres appear to be diminished in number, and there is no indication whatever of any tract degeneration. We think that the slight general interstitial overgrowth which is present is probably not unlike the fibrotic condition occurring in many organs as a result of old age; such a condition is not at all uncommon in the spinal cords of old people.

Anterior Roots.—The anterior nerve roots in the cervical and lumbar regions are much atrophied.

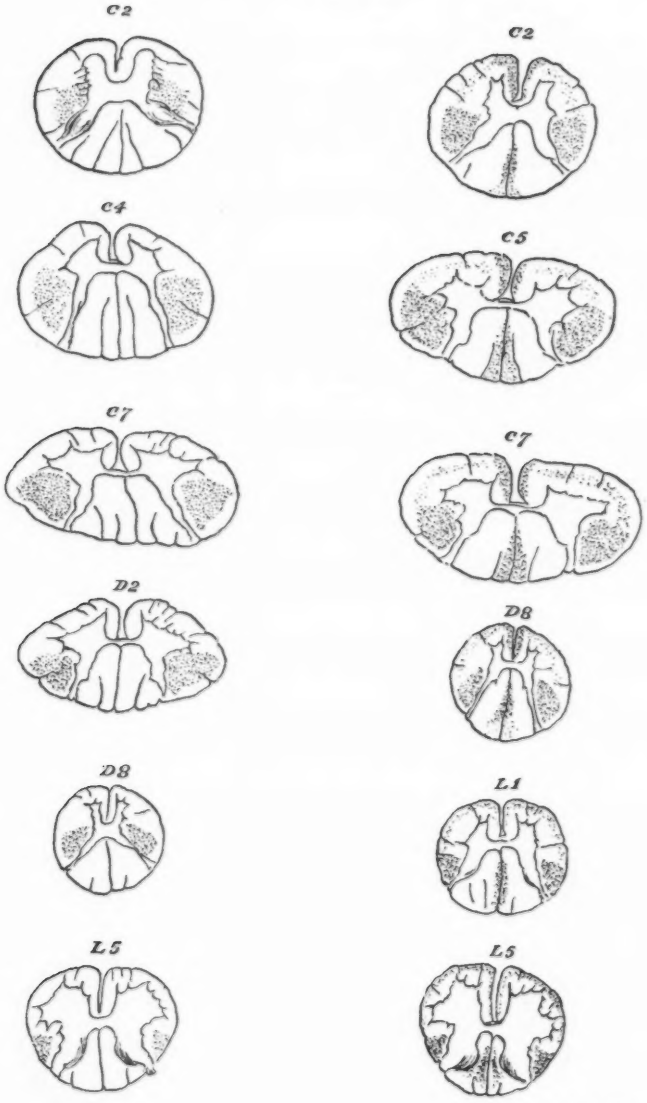
Vessels.—Most of the small and medium-sized vessels are in the condition described by Gull and Sutton of arterio-capillary-fibrosis; those of the peripheral nerves and skin also show the same change.

The *membranes* are not thickened, and appear fairly normal.

Spinal ganglia.—Several were examined from the lumbo-sacral enlargement. Marchi sections show no fatty degeneration, but the cells contain an abundance of black pigment in small granules. Nissl-stained sections show that many of the cells are somewhat shrunken and shrivelled, and the pigment in these sections is yellow in colour. There is, however, no very definite degeneration, and nothing of an acute nature. There is a slight increase of the fibrous tissue throughout the ganglia.

Peripheral nerves.—The right and left great sciatic and ulna nerves were examined in longitudinal and transverse

PLATE I.

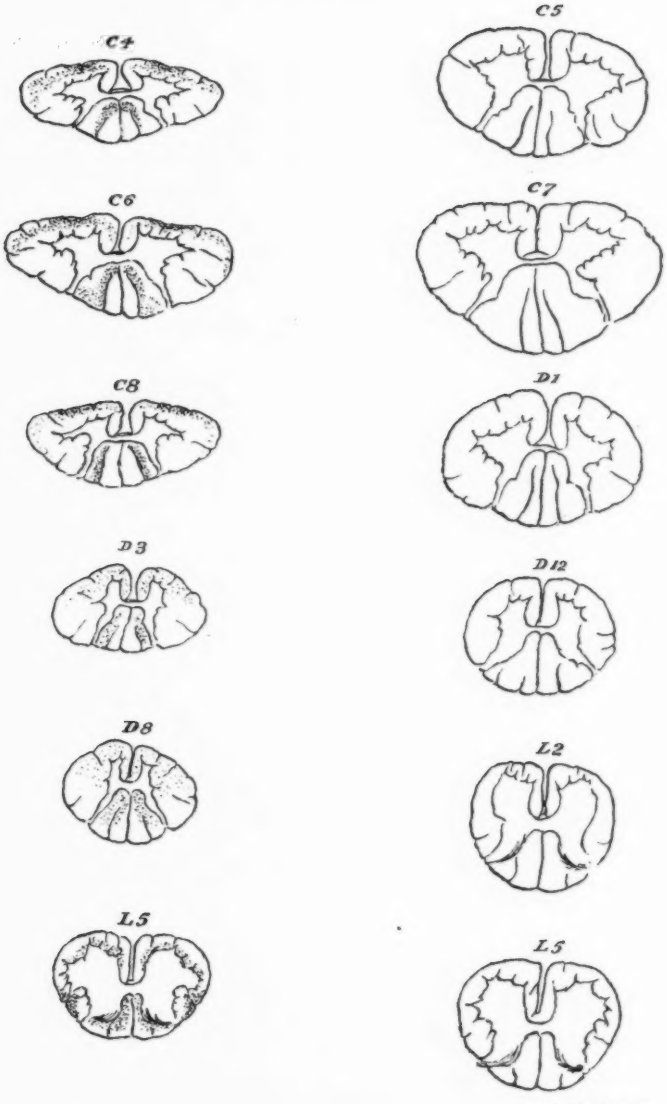


A. F. Tredgold, del.

CASE NO. 1.

CASE NO. 2.

PLATE II.



A. F. Tredgold, del.

CASE NO. 3.

CASE NO. 4.

sections. In the Marchi preparations there appears to be considerable diminution in the number of fibres, but there is no recent degeneration. In sections stained by the carmine-Weigert method it is readily seen that there is a considerable deficiency in the number of fibres. In the transections of some of the bundles there are quite large areas, as much as one quarter of the section, almost entirely devoid of nerve-fibres, their place being taken by an overgrowth of connective tissue.

Thumb muscle.—A section of this stained by Marchi's fluid, shows that there are a few fibres in which striation is well marked, and which appear to be quite healthy; but a still larger number are cloudy looking, and their striation is indistinct, although they do not show any fatty change; others, however, are in a typical condition of fatty degeneration.

We have considered it advisable to include this case, since the microscopical appearances almost exactly agree with those in the three preceding ones; the cells and fibres undergo exactly the same chronic atrophy, there is just the same increase of pigment, and just the same thickening and fibrosis of the vessel walls. In one respect there is a difference; it has been seen that in the other three cases the mesial-anterior group of cells in the anterior horns is comparatively little affected, the chief change being in the lateral groups; in this case, however, there are as many atrophied cells in this group as in any other. We are unable to say whether the change in the anterior horn cells is primary or secondary to the joint change, or to give any satisfactory explanation of this difference, we simply record the fact.

Remarks.

Degeneration of the motor tract is the anatomical lesion present in several diseases having distinct clinical features. Thus it occurs in Friedreich's disease, in combined lateral and posterior sclerosis, and in general paralysis; but in these other neuronic systems are also affected. Degeneration of the motor path may also be the result of a local lesion, *e.g.*, anterior polio-myelitis, polio-encephalitis, embolus, &c.; and

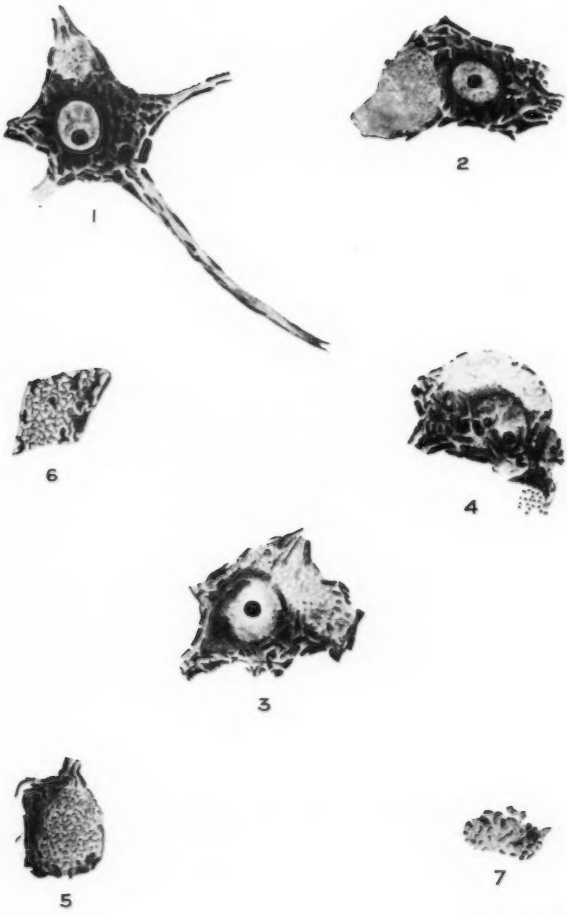
lastly, cases exist in which not a degeneration, but an arrest of the development of the efferent tract occurs, apparently due to a simple agenesis; these cases are usually associated with microcephaly.

On the other hand, there are instances in which the motor tract undergoes a *primary degeneration*, neither the result of a localised lesion nor part of a more general disease; clinically this may appear as amyotrophic lateral sclerosis, progessive muscular atrophy, primary spastic paraplegia, or bulbar paralysis. It is with such primary degeneration that the present paper deals, it must, however, be remarked that as the *result* of the change in the motor path, other conducting tracts may be affected.

(I.)—*The Nature of the Morbid Process.*

There is every reason for considering the change in these cases to be a subacute or chronic degeneration of a portion or the whole of the motor tract, that is, of the upper segment alone, of the lower segment alone, or of both segments together. The cases which have just been described in detail demonstrate that the change is a slow decay of individual neurones. In no instance could we find any evidence of acute change in the cells, and it may be remarked that also in the nerve-fibres and in the muscles the process is usually one of gradual atrophy, with very little appearance of true fatty degeneration like that met with in acute processes. The cells become shrunken and irregular in outline; the Nissl bodies gradually disappear, their place being taken by a large collection of yellow pigment which stains black with Marchi's fluid; the nucleus becomes smaller and its outline indistinct, later it is displaced to the periphery of the cell, and at last disappears; the processes get much thinner and eventually break off; and finally a small mass of granular pigment is all that is left. These successive changes are shown in Plate III. which is drawn from cells stained by Nissl's method. The nerve-fibres and their end-organs, the muscle fibres, wither away in the same manner; in the muscles a true fatty degeneration does in some instances occur, and fibrils may be seen in

PLATE III.



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Showing the stages of degeneration of an anterior horn cell.

To face page 426.

this condition, but very often the individual fibres gradually become thinner, their striation disappears, and they are finally replaced by connective tissue. In longitudinal sections of the peripheral nerves we have at times come across small portions of naked axis cylinders; in transverse sections the diminution in the number of fibres, and increase in the connective tissue is particularly well seen. Neuroglia gradually takes the place of the atrophied nerve-fibres in the central nervous system, causing a sclerosis which is secondary and not primary.

The process is therefore slow, but progressive, and the best explanation which can be offered of its occurrence is that the neuron has reached that stage at which its inherited vitality is exhausted, and it is no longer capable of performing the metabolism necessary to its life. The presence of intracellular pigment which is almost universal in these cases is probably an indication of presenile decay. Various theories have been put forward to otherwise explain the condition, thus by some it has been thought to be due to a toxic influence, but although there can be no doubt that certain poisons have a selective action upon certain neuronic systems, there does not appear to be any evidence in support of this view in these cases; the changes in the cells are entirely unlike any toxic condition with which we are acquainted. Neither can vascular alterations be looked upon as the primary cause of the disease; it is true that in a very large proportion of these cases structural changes in the vessel walls are found (arterio-capillary-fibrosis), but these vascular changes are present throughout the entire nervous system, and in many cases other parts of the body also, so that it is unlikely that the degeneration would be confined to the efferent tract unless there existed a tendency to premature decay on the part of its neurons. It is possible, however, that the vascular alterations, by bringing about an inadequacy of the circulation, may act as a contributory factor. The age at which these diseases begin (a time when the motor system is usually in full vigour) and the fact that several members of a family may be similarly affected, lend considerable support to the view of hereditary

influences. It may be asked: Is the degeneration of a particular system of neurons entirely due to these tendencies, or may the site of the disease not be determined by some external cause? It has been repeatedly pointed out by one of us that in tabes, for example, the initial site may be brought about by occupation, &c.; thus, in those whose work entails constant stress upon the lumbo-sacral region of the cord, this is the part first affected, whilst in others in whom the arms are chiefly used, the disease begins in the upper part of the cord.* It is therefore likely that in the cases we are now considering the occupation of the patient may determine which *portion* of the efferent tract will be first affected, but there does not seem to be any reason for thinking that the selection of the *tract* itself (whether afferent or efferent) can be so influenced; such must be due to hereditary predisposition. It should be remembered that excessive motor sense impressions are but the outcome of excessive movements, and that the one is commensurate with the other; the stress on both systems is therefore equal.

With regard to the morbid anatomy of these diseases (especially amyotrophic lateral sclerosis), it has been frequently noticed that in some instances the sclerosis in the pyramidal tracts cannot be traced higher than the medulla or pons, in others as far as the crura, and in others up to the internal capsule, although most observers have been able to find evidence of change, in the presence of granular bodies, as high as the motor cortex. There are, of course, many difficulties in the way of demonstrating sclerosis higher than the capsule, but even allowing for this there can be no doubt that it is frequently more pronounced in the most distant part of the efferent tract. The explanation of

* The cab-driver would use his legs but little, his arms and hands a great deal in driving and lifting the boxes on and off his cab, hence the limitation of the disease in Case 3. Two other examples occurred in the practice of one of us (F. W. M.). A cooper, who wielded a 4 lb. hammer, was affected first in the right arm with amyotrophic lateral sclerosis; but an Italian waiter was affected first and most severely in the muscles of the left hand and shoulder; upon being asked whether he could in any way account for this, he said he carried a tray all day long with his left hand. The familiar figure of the waiter of the Italian restaurant with the loaded tray poised on the left hand, level with the shoulder, suggests stress on the very muscles which were first affected in this man.

this is easier if we remember that the change is not an acute one like that resulting from a focal lesion, but that a slow and gradual death takes place, the parts most distant from the cell being the first affected.

We may here describe a case which affords a microscopical demonstration of this point:—The patient had well-marked hemiplegia and aphasia, due to thrombosis of the left middle cerebral artery, death taking place on the twelfth day. The cells of the cortex were stained by Nissl's method, but after examining many sections it was found to be quite impossible to distinguish between those of the two hemispheres, that is to say, no departure from the normal could be detected in the pyramidal or other cells of the left motor region, although the patient was quite hemiplegic. On examining the pons and medulla there were found to be definite alterations in the efferent tract. At this level there was little (scarcely any) Marchi degeneration (what was present was confined to small fibres, possibly collaterals, and therefore almost terminal ones); many of the large fibres, however, were greatly swollen, and appeared to be in a condition of coagulation necrosis. There were no similar fibres in the corresponding region of the other side. Still lower down, in the cervical cord, many fibres were seen in a typical condition of fatty degeneration in the left direct and right crossed pyramidal tracts. Thus it is seen that in these cases of gradual death of the neuron, degeneration *simultaneously throughout the course of the fibre does not take place;* the fatty change begins in the most distant part of the fibre, and then ascends towards the cell; this fatty change being preceded by a swollen condition of the axone.

This case affords an explanation of the peculiar microscopical appearances which have been observed in amyotrophic lateral sclerosis, and why it is that although degenerative changes are always well marked in the distant portions of the tract, they become less evident in the higher regions. Occasionally, if the case is of considerable standing, definite degeneration may be found in the motor cortical cells, as in Case No. 1.

Marie drew attention to the fact that in cases of amyo-

trophy emotional disturbances frequently exist. Our own experience entirely confirms this, the patients very generally showing a ready tendency to burst into tears, or, less often, into laughter, for slight causes. There is psychomotor slowness in the emission of ideas, the memory and attention are not lost, but dormant, and require an effort to be revived. There is no true dementia, however, and this is in accordance with the fact that in the cortex the degeneration is confined to the large Betz cells; *the smaller and medium-sized pyramids and the layers of tangential and superradial fibres being quite unaffected.* This constitutes a very important microscopical difference between this condition and those of general paralysis and senile dementia associated with degeneration in the efferent tract. Sometimes in amyotrophy a slight thickening and opacity of the pia-arachnoid membrane over the motor cortex may be found, which, in view of the limitation of the degeneration, must certainly be looked upon as secondary. Pierret considers that there is a close relationship between general paralysis and amyotrophic lateral sclerosis.

(II.).—*The Pathological Relation between the Upper and Lower Motor Segments.*

Charcot maintained that in cases of amyotrophic lateral sclerosis, the primary lesion was a degeneration of the pyramidal tracts, and that this caused a "deuteropathic" affection of the ganglion cells of the anterior horns. Sir Wm. Gowers and Leyden strongly object to this view, and consider that a primary and independent degeneration takes place throughout both the upper and lower segments, the change in one not being brought about by that in the other, but both being due to a common cause; indeed, they consider that in by far the larger number of cases, both segments are affected simultaneously, and that it is extremely rare to find, in cases of progressive muscular atrophy, an absence of change in the pyramidal tracts also.

In support of Charcot's view, it must be admitted that a degeneration of the pyramidal tracts resulting, say, from a

cortical lesion, may be followed by changes in the anterior horn-cells. Schäffer, in a case of cerebral hemiplegia of short duration, found chromolytic changes in the postero-external group of anterior horn cells, which he regarded as secondary to the degeneration of the pyramidal tracts. Marie thinks that diminution in the size of the anterior horn is almost always present in long-standing cases of degeneration of the pyramidal tract. Fürstner and Knoblauch also noted the same thing, and pointed out that it was the lateral cell groups which were chiefly affected.

The different kinds of birth palsies also show that degeneration or arrest of development of the upper efferent tract may bring about very important changes in the cells and fibres of the lower tract. In a recent article we described three such cases of primary cerebral lesion, and in each of them, in addition to the atrophy of the corresponding pyramidal tract, there was marked diminution in the anterior horn cells of the arm and leg enlargements, and atrophy of the peripheral nerves and muscles.

One also at times sees in cases of hemiplegia occurring in middle age a very considerable wasting and flaccidity of the muscles which are rendered paralysed. A large part of such may very probably be the result of disuse, but in some cases this explanation seems by no means adequate and in these it almost looks as if the upper segment did really exercise a kind of trophic influence over the lower. It must be admitted that this only takes place after the lapse of some considerable time; the subject is, however, one well worthy of further attention. There can be no doubt that the *afferent* fibres exert a trophic action upon the anterior horn cells. Warrington found chromolytic changes in certain of these cell groups after section of the posterior roots, which he attributed to the withdrawal of afferent impulses normally acting upon these cells in the production of reflex spinal tonus.

Whilst therefore there can be no doubt of the existence of a trophic action between the upper and lower parts of the efferent tract in some cases, the presence of degeneration in one portion resulting from degeneration in the other seems

to be rather the exception than the rule, and it is now well established that disease may involve either segment separately, or both together. In Case No. 4, although the condition is perhaps not strictly a primary degeneration of the lower segment, the change is confined to that segment, and in spite of its duration of several years there is no evidence of implication of the upper portion of the tract. There have also been a few cases recorded (by Strümpell and others) of the opposite condition, the degeneration being limited to the pyramidal bundles and the anterior horns showing no change (primary spastic paraplegia). One also not infrequently meets with similar cases of a temporary nature, in which spastic paraplegia is present, the patellar reflexes being greatly exaggerated, as a rule recovery takes place after a longer or shorter time, and hysteria is often invoked as the cause; but many such cases may be directly traced to an infectious process, such as influenza, &c. On the other hand there are certain poisons, of which diphtheria is a well-known example, which seem to have a special predilection for the lower segment. If, therefore, each segment of the motor tract is specially susceptible to the influence of particular poisons, it seems legitimate to conclude that there also may be different hereditary tendencies present in the two tracts. In some persons there may be a tendency to premature decay in the upper portion, in others in the lower portion, and still in others throughout the entire motor system.

(III.).—*The Involvement of other Neuronic Systems.*

Many writers would exclude from the cases we are now considering those in which other tracts than the efferent are affected; but although we most certainly hold to the view that a degeneration in the motor system is the primary and essential change, and that in many cases no other tracts are affected, it is certain that in a not inconsiderable number of cases (amyotrophic lateral sclerosis in particular) atrophic changes also exist in other tracts of the white matter. Such changes, however, are to be looked upon rather as secon-

dary in nature than as a true primary degeneration like that occurring in the pyramidal tracts. These secondary changes take place in two distinct systems—*i.e.*, association and afferent.

Association fibres.—As is well known, the anterior horn-cells of different segments of the spinal cord are brought into communication with one another by means of short and long association systems. Many of the short fibres probably do not leave the gray matter, but the longer ones occupy the antero-lateral columns lying intermediate between the periphery of the cord and the gray matter of the horns. In many cases of amyotrophic lateral sclerosis and of progressive muscular atrophy a well-marked band of interstitial sclerosis is to be seen in this region, indicating the involvement of these fibres. Osler also mentions a case in which sclerosis occurred in the medial longitudinal bundles, which are generally thought to convey association fibres from the cord to the medulla and pons. It is likely that the very great disappearance of fibres from the network of the anterior horns is partly due to atrophy of short association fibres; it certainly cannot be entirely due to affection of the terminal filaments of the pyramidal tracts as might be supposed, because in Case 4 the diminution in this network is almost as marked as in the other cases, and yet in this the upper efferent tract was not involved. These association systems are evidently part of the *lower* motor segment; they undergo no change if the degeneration is confined to the upper segment (as in hemiplegia, &c.), and their atrophy appears to be proportional to the number of anterior horn-cells affected; possibly it is of a secondary nature, and due to the fact that they are put out of action by the death of the anterior horn-cells, which they usually serve to connect. According to the view of von Monakow, which is supported by Schäfer's experimental operations, the terminal arborisation of the pyramidal systems does not come into direct connection with the dendrons of the spinal motor neurons, but through the intervention of intercalary neurons of the second type of Golgi.

The opposite halves of the cord are similarly connected

by fibres passing through the anterior commissure, and in most cases there is a very well-marked sclerosis in this region also.

Afferent fibres.—Charcot, Pierre Marie, and other observers have drawn attention to the fact that in amyotrophic lateral sclerosis the *posterior* columns are frequently sclerosed, and although this has been denied by other writers, our experience certainly confirms it. The extent of this change in our cases will readily be seen by a reference to Plates I. and II., and to the description of the cases. We were also able to demonstrate atrophy of some of the fibres of the posterior roots. It must therefore be admitted that changes do occur in the afferent tracts; the explanation, however, is not easy, and there seems to be no recorded instance of atrophy of any other portion of the afferent system than the posterior columns. All writers agree that the cells and reticulum of Clarke's column, the direct cerebellar and the ascending tracts in the antero-lateral column are unaffected. We suggest the following explanation of this atrophy of posterior column fibres. These fibres convey impressions arising in the deep structures, especially the muscles; in support of this statement we may refer to Sherrington's important observation that one-third to one-half the fibres entering muscles are afferent. It is highly probable that other sensory impressions (tactile, pain, and temperature) which come from end organs situated in the skin and subcutaneous tissues are conducted by the short fibres which enter the gray matter of the cord immediately, terminating in an arborisation around cells of the substantia gelatinosa of the posterior horn. In degenerations of the motor tract, although the muscles are profoundly atrophied and in many cases converted into little more than fibrous tissue, the overlying skin remains unaffected, and the ordinary sensations are not interfered with; it therefore seems possible to look upon the change in the posterior columns as being due to the secondary disuse atrophy of fibres coming from the muscles. We know that similar changes take place in *all* the afferent tracts after amputation of a limb; we have ourselves observed

this in several such cases, and this view explains why, in wasting of the muscles only, such change should be confined to the posterior columns.

In addition to these secondary alterations in tracts, some cases, especially those of long duration, show a diffuse increase in the interstitial tissue throughout the cord, the septa and adventitia of the blood-vessels being also much thickened. It is not uncommon to find this condition in other cases of chronic nervous degeneration, and also in old age.

References.

(1) Charcot, J. M. Leçons sur les Maladies du Systeme Nerveux.

(2) Leyden and Goldscheider. "Die Erkrankungen des Rückenmarkes."

(3) Gowers, Sir Wm. "Diseases of the Nervous System."

(4) Marie. "Les Maladies de la Moelle Epinière."

(5) Pierret. "Sclérose Systématique du Tractus Moteur," Extrait du *Volume du Centenaire de la Société de Biologie.*

(6) Schaffer. *Monatschrift für Psychiatrie und Neurologie*, 1897.

(7) Fürstner and Knoblauch. "Ueber Faserschwund in der grauen substanz und über Kerntheilungs-vorgänge im Rückenmarke unter Pathologischen Verhältnissen," *Archiv. f. Psych. und Nervenkrank*, Bd. xxiii., H. i. Ref. *Neurol Centralblatt*, 1891.

(8) Mott. "A Case of Amyotrophic Lateral Sclerosis with Degeneration of the Motor Path from Cortex to Periphery," *Brain*, 1895.

(9) Warrington, W. B. *Journal of Physiology*, vol. xxiii., 1898.

(10) Sherrington. Muscle Sense, "Text-Book of Physiology." Schäfer.

(11) von Monakow. "Ueber den gegenwärtigen stand der Frage nach der localization im Grosshirn. Separat Abdruck aus Ergebnisse der Physiologie."

(12) Schäfer. "Essentials of Histology," 1902.

ON THE PALLIO-TECTAL OR CORTICO-MESENCEPHALIC SYSTEM OF FIBRES.

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Introduction and Method.

In the course of an investigation of the fibres composing the crus cerebri in a number of animals (twenty cats, eleven monkeys, one dog, and two badgers) localised lesions in the pallium or cortex cerebri had been made by one of us (V. H.). While tracing the degenerations which resulted from such lesions we have specially followed out the connections which have for some years been known to exist between the cortex cerebri and the mesencephalon. In all cases the procedure was the same. A small area of the cortex in an animal anæsthetised with ether or chloroform was either excised or separated by a tangentially-directed incision through the corona radiata, so as to undermine the part determined upon.

Antiseptic precautions were always taken, and at the end of three weeks the animal was chloroformed, bled to death, and the vessels were washed out with Muller's fluid. The whole encephalon when fixed was cut into slabs, stained by Busch's modification of the Marchi method, and cut in serial sections. Only cases of healing by immediate union were accepted.

History.

The former investigations on this question may be grouped chronologically as follows:—

In 1891 the pathological observations of Zacher[1] on man,

[1] *Archiv. für Psych.*, Bd. xxii., 1891, p. 654.

though necessarily indeterminate owing to the length of time elapsing between the occurrence of the lesion and the death of the patient, appeared to indicate that fibres pass from the occipital cortex to the mesencephalon by the lateral segment of the cerebral peduncle. His cases also suggest that the corpus geniculatum internum and the inferior corpus quadrigeminum were in connection by fibres with the cortex, and possibly with that of the temporal lobe.

In 1895 Edinger[1] first proved by the degeneration method in the bird the occurrence of an occipito-mesencephalic tract. The fibres proceeding from the occipital pole of the bird's hemisphere pass dorsally to the basal-frontal bundle and end in the deepest layers of the mesencephalon. The lesion was an extirpation of the "occipital" pole, and it extended forward to involve slightly the posterior part of the basal ganglia.

In the same year (1895) Boyce[2] showed that after removal in the cat of the anterior third of one cerebral hemisphere there was in the middle region of the optic thalamus a group of scattered large degenerate fibres leaving the internal capsule and entering the optic thalamus, where they were grouped around the lower and inner aspect of the ventral lateral geniculate body. In more posteriorly-made sections they passed backward beneath the pulvinar and came to the surface as a well-marked group immediately external to the anterior corpus quadrigeminum. Some of these fibres entered the base of the corpus on the same side as the lesion, and probably some fibres terminated here; others he observed to cross over in the roof of the aqueduct to the opposite side, where they possibly terminated in either of the corpora quadrigemina. Fibres could also be traced back to the quadrigeminal region, being given off from the degenerate fibres in the capsule during their course to form the crusta. One well-marked bundle passed from the upper and incurved extremity of the pyramid just before the crusta is formed to the roof of the aqueduct, and lower down isolated fibres came off from the outer and upper extremity

[1] "Ueber die Entwickelung des Rindensehens," *Archiv. für Psych.*, Bd. xxvii., 1895, p. 950.

[2] *Phil. Trans. Roy. Soc.*, vol. 188, Series B, 1895, p. 335.

of the crusta and curved round to the quadrigeminal region. Small groups of fibres left the dorsal and inner portion of the pes pedunculi and passed back to the tegmental commissural region of the same side, but whether they actually crossed over in the posterior commissure to the opposite side was not proved.

Lower down also he found that degenerated fibres left the crusta and passed back to the quadrigeminal region of the same side.

According to Dejerine[1] the radiations of the anterior corpus quadrigeminum, *i.e.*, tecto-pallial fibres, pass above and in front of the corpus geniculatum externum which they separate from the posterior segment of the internal capsule, and particularly from the bundle of Turck in front of the corpus geniculatum internum, and between this last and the pulvinar. Then they become superficial while running together to form the brachium of the anterior corpus quadrigeminum, and they spread out finally into the superficial and middle layers of the anterior corpus quadrigeminum.

Simpson,[2] in 1901, observed fibres in several cats in which "an attempt was made to divide the projection fibres arising from the left motor cortex in its whole extent." He observed fibres from the posterior aspect of the crusta passing back through the tegmentum and ending in the homolateral superior colliculus,[3] a few crossing to the contra-lateral colliculus, while in addition a fine degeneration was also observed in the locus niger. In the dog and monkey he found no such fibres.

Results of the Present Research.

(1) *General Statement.*

As the present research is founded chiefly on observations on the cat as representing the carnivora, and the macacque monkey (usually *Macacus rhesus* and more rarely *Macacus*

[1] "Anatomie des Centres Nerveux," Tome ii., Fasciculus 1, 1901, p. 70.
[2] *Journal of Physiology*, vol. xxvii., 1901, p. 11.
[3] The terms superior and inferior colliculus instead respectively of anterior and posterior corpus quadrigeminum, though not in general use, appear to deserve general adoption as being more succinct.

sinicus) as representing the Primates, it will be understood that a general statement is only completely applicable to the higher of these animals, in which there is a well-developed non-excitable area (frontal) in front of the so-called motor or excitable cortex. With this proviso the general scheme of a pallio-tectal system may be stated as follows :—

From the frontal cortex no fibres could be traced by us to the mesencephalon ; from the temporo-sphenoidal cortex very few fibres; while from the occipital lobe a fair number, and from the excitable cortex a large number of fibres can be followed to the corpora quadrigemina and mesencephalon.

The course taken by the different groups of fibres may now be detailed, and as the occipito-mesencephalic group is somewhat special by reason of the highly-developed visual association between the cortex of the cuneal region and the superior colliculus (anterior corpus quadrigeminum) we will describe that first.

(1) *Occipito-Mesencephalic Fibres.*

The results we have obtained from the occipital lobe are strikingly concordant and fully confirm Edinger's original generalisations on this subject.

In proportion as more of the area of cortex containing Gennari's[1] streak is involved in the lesion the number of degenerated fibres passing to the colliculus increases.

The occipital lesions produced in the present investigation were all situated on the outer surface of the pallium.

In one observation in the monkey we made a small lesion involving the posterior lip of the "affen-spalte," to which Gennari's streak reaches in *Macacus rhesus*. From even this small lesion, some fibres passed to the anterior colliculus, showing how complete the association between the occipital area and the mesencephalon is.

The fibres which descend from the occipital cortex to the superior colliculus are large and stand out distinctly from the medium-sized occipito-thalamic and occipito-geniculate fibres and from the small callosal fibres and fine collaterals

[1] The comparative morphological topography of Gennari's streak is not yet worked out, but we have accumulated a large mass of material on which the statement above is based.

which enter the corona radiata in large numbers. Some of the occipito-tectal fibres pass among the fibres composing Gratiolet's radiation, others run through the mesial region of the inferior longitudinal bundle (posterior fourth). This is in harmony with the converse observations of Schütz, made on microgyric brains, in which fibres of the inferior longitudinal bundle were found to be really tecto-occipital in character.

In traversing the thalamus the occipito-mesencephalic fibres run for the most part in the stratum zonale, but also partly through the lateral part of the dorsal nucleus.

A very few pass just mesially to the corpus geniculatum internum, and all are distributed to the whole breadth of stratum griseum profundum of the anterior colliculus.

(2) *Temporo-Mesencephalic Fibres.*

It will be better to divide the results from lesions of the temporal lobe, according to the animals, cat and monkey, operated on, because the homologies of the gyri in two so distant genera have not yet been accurately determined.

(*a*) Cat.—The terminology descriptive of the temporal gyri in the cat is best given in Flatau and Jacobsohn's [1] handbook. We have made lesions in the small gyrus behind the Sylvian fissure, *i.e.*, the gyrus Sylviacus posterior and in the next gyrus behind it, viz., the gyrus ecto-Sylvius posterior. Of these two, injury of the former only reveals fibres passing to the locus niger. Lesion of the posterior limb of the ecto-Sylvian gyrus demonstrated an outflow of the fibres both large and small passing to the mesial side of the posterior extremity of the lenticular nucleus entering the outermost bundles of the internal capsule, and thence distributed to (*a*) the optic thalamus, (*b*) the corpus geniculatum internum, (*c*) the posterior brachium of the corpora quadrigemina (colliculi), (*d*) the pontine nucleus. Of these it is to be noted that a number of fibres in the posterior brachium turn up towards the posterior colliculus, but we have never been able to follow them into that ganglion; that

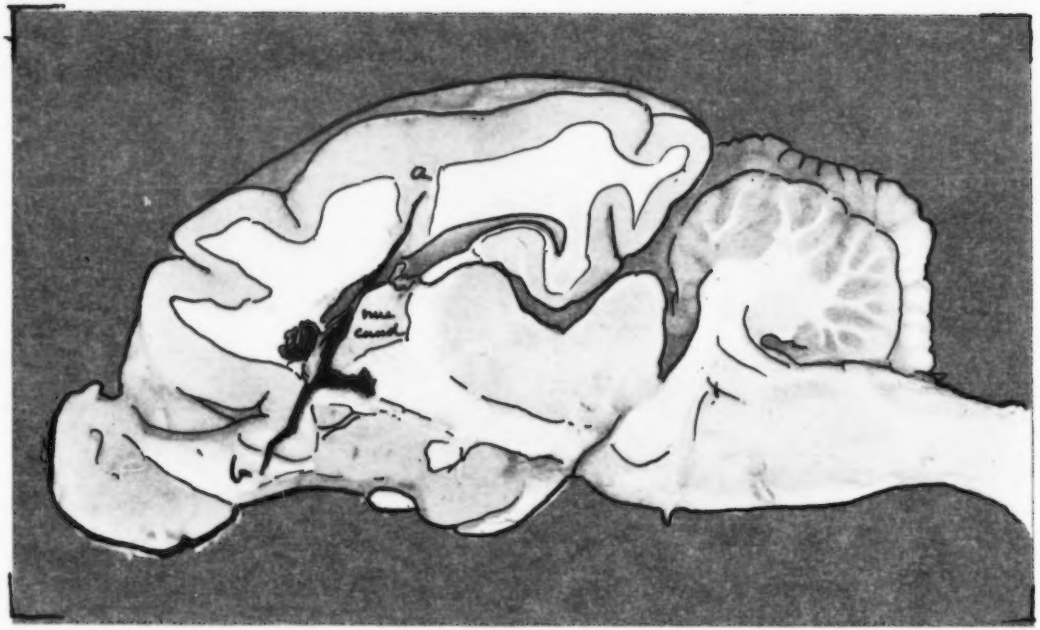
[1] "Handbuch der Anatomie und Vergleichenden Anatomie des Centralnervensytems der Säugethiere." 1899.

FIG. 1.

Pallio-tectal fibres from localised lesion of parietal cortex. Sagittal section at 45° to the vertical plane. Cat. Marchi prepn.

(*a*) Pallio-tectal fibres in corona radiata passing back to cross the posterior limb of the internal capsule.
(*b*) Do. traversing lattice layer and lateral nucleus of thalamus.
(*c*) Do. curving mesially to corpus geniculatum internum to enter the superior colliculus and posterior brachium.

FIG. 2.



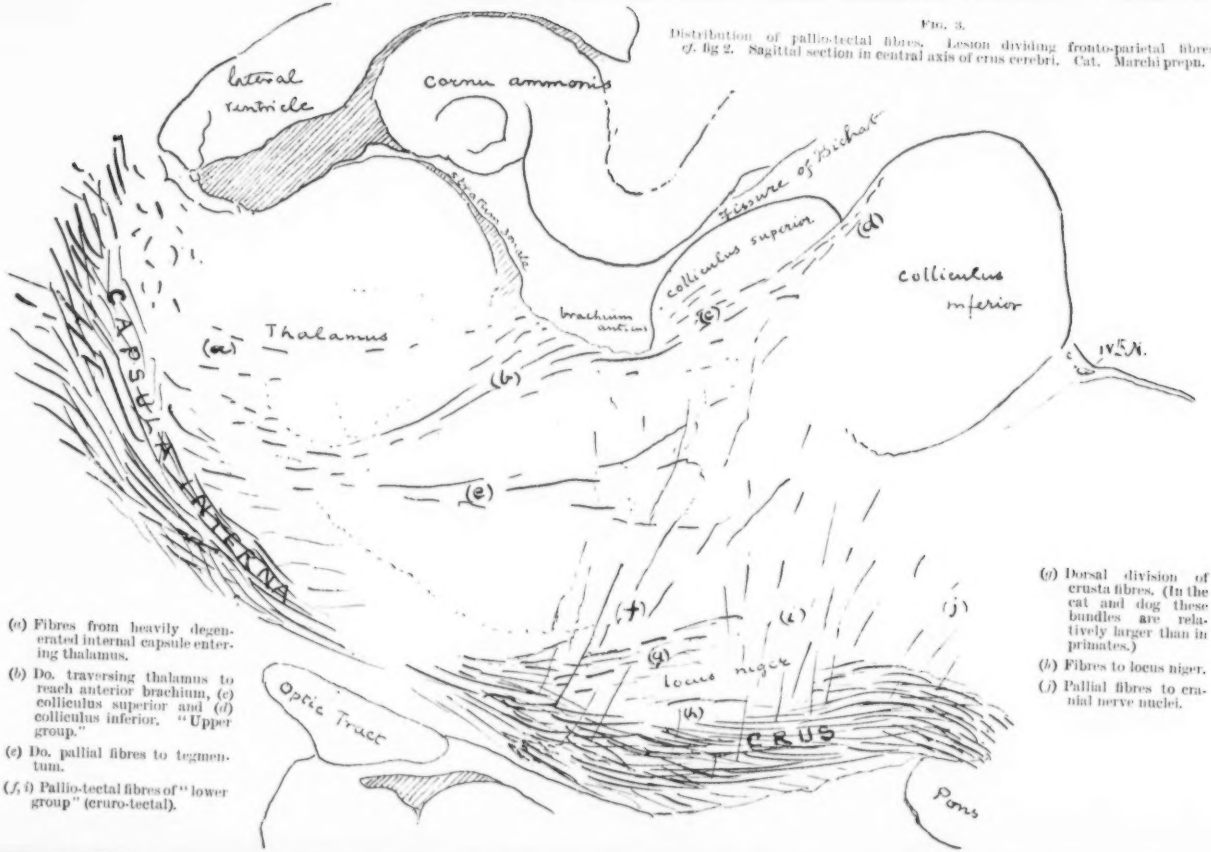
a b—Line of lesion producing maximal degeneration of fronto-parietal pallio-tectal fibres. Cat. Injury to the nucleus caudatus does not add to the number of tectal fibres. This figure is in a plane about one millimetre outside that of fig. 3.

Fig. 5.

a—Line of lesion producing maximal degeneration of fronto-parietal pallio-cortical fibres. (Mz.
injury to the nucleus caudatus does not add to the number of cortical fibres.
This figure is in a plane about one millimetre outside that of fig. 3.

FIG. 3.

Distribution of pallio-tectal fibres. Lesion dividing fronto-parietal fibres, *cf.* fig 2. Sagittal section in central axis of crus cerebri. Cat. Marchi prepn.



(*a*) Fibres from heavily degenerated internal capsule entering thalamus.

(*b*) Do. traversing thalamus to reach anterior brachium, (*c*) colliculus superior and (*d*) colliculus inferior. "Upper group."

(*e*) Do. pallial fibres to tegmentum.

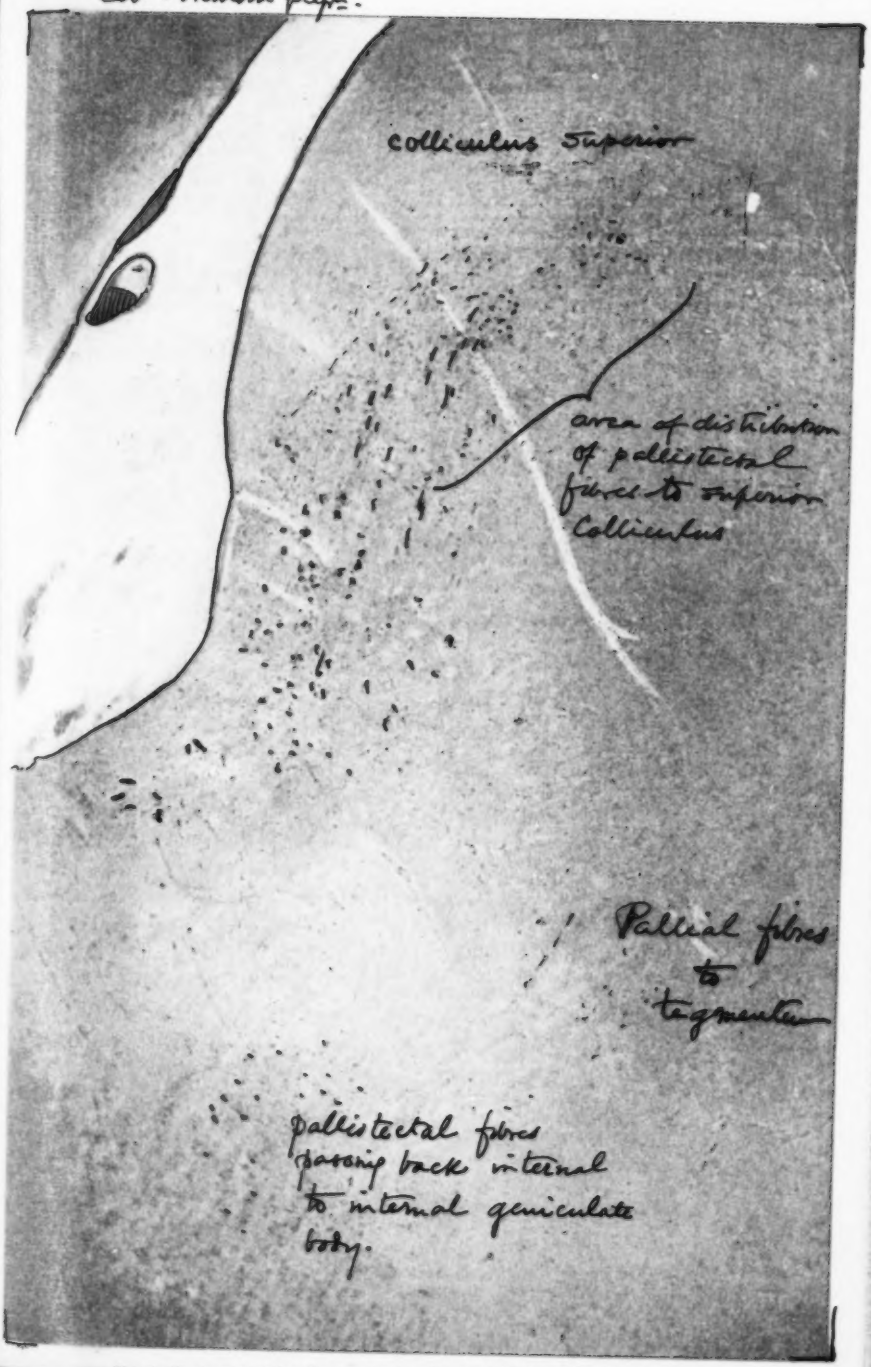
(*f*, *i*) Pallio-tectal fibres of "lower group" (cruro-tectal).

(*g*) Dorsal division of crusta fibres. (In the cat and dog these bundles are relatively larger than in primates.)

(*h*) Fibres to locus niger.

(*j*) Pallial fibres to cranial nerve nuclei.

Cat. Marchi preps.


colliculus superior
area of distribution of pallistectal fibres to superior Colliculus
Pallial fibres to tegmentum
pallistectal fibres passing back internal to internal geniculate body.

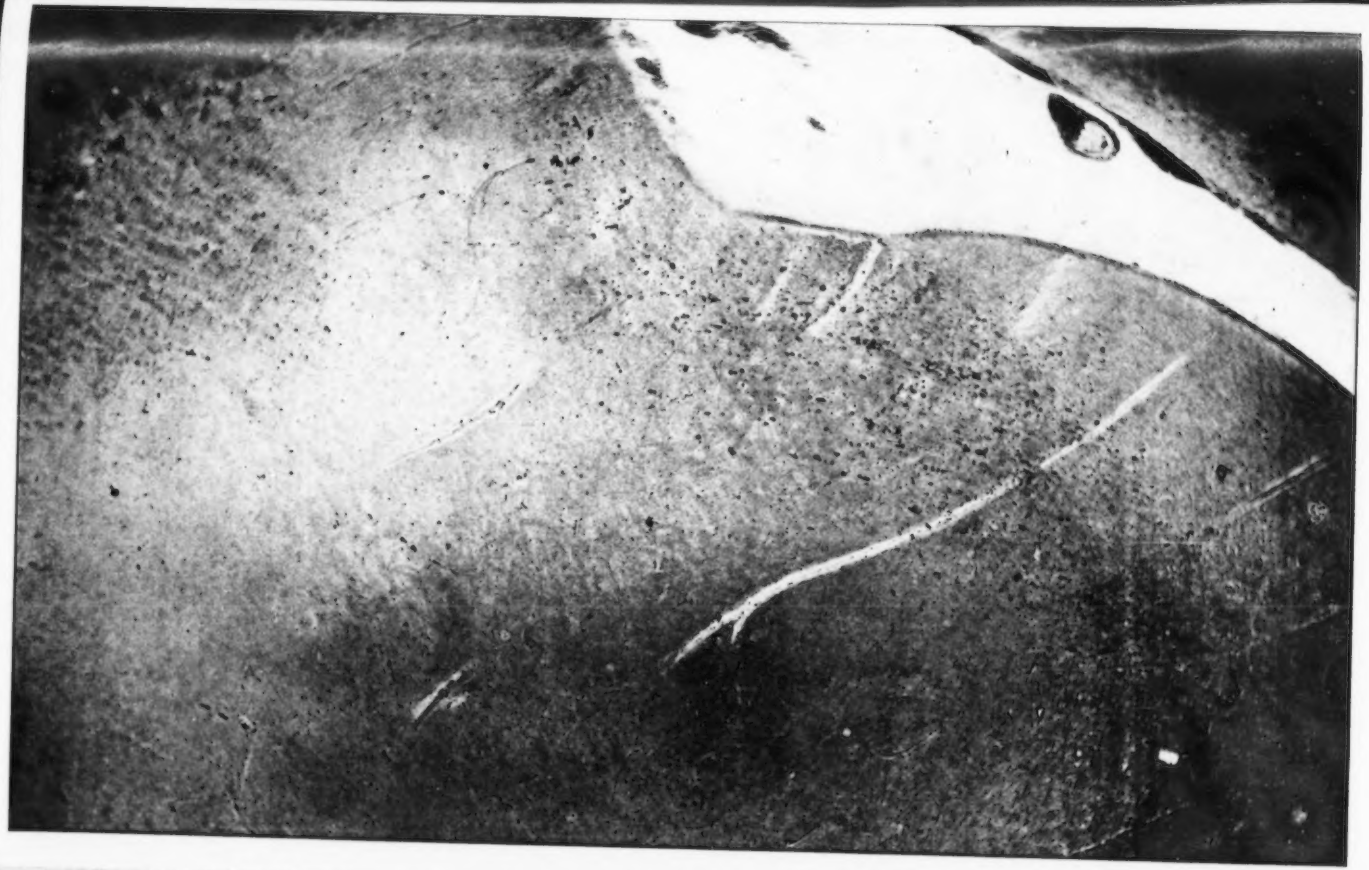
Cr. Marine ridge.

collinulus superior

area of distribution of peliti terrel three of superior collinulus

Pelicil shire of Tasmania

Pelicil terrel shire showing track in terrel & in terrel peninsulate body.



is, we have never been able to follow them beyond the gray matter forming the anterior fused border of the nucleus of the lateral fillet. The fibres which pass to the brachium are accompanied in the first part of their course by the fibres to the internal geniculate body. The fibres to the pons run down on the outside of the crus as Dejerine[1] has shown in man, and terminate in the upper and outer part of the frontal extremity of the pontine nucleus. In this animal (cat) they cannot be traced for a greater distance than one-third of the antero-posterior length of the pons.

(*b*) Monkey (*Macacus rhesus*).—Of the lesions which we made in the temporal gyri, all involved the posterior half of the gyrus operated upon.

In all cases fibres were traced to (*a*) the thalamus opticus, (*b*) the corpus geniculatum internum, (*c*) the posterior brachium, and (*d*) the locus niger. These fibres for the most part are of fine or medium size, and they appear to be coarser in proportion as they arise from cortex which was nearer to the Sylvian fissure.

(3) *Parieto-Mesencephalic and Combined Fronto- and Parieto-Mesencephalic Fibres.*

The fibres coming from the excitable cortex we have investigated in two ways, either by producing a small lesion in a localised area of the so-called motor region, or by division of the corona radiata so as to undermine selected gyri, or by an extensive incision which was carried vertically through the hemisphere so as to separate the anterior third or half more or less completely.

The results of these experiments will best be described as before, under the denomination of the animal investigated.

(*a*) Monkey.—In this animal the system of fibres connecting the excitable area with the mesencephalon is relatively only moderately developed, and was not in fact observed by Simpson in the two animals which he examined.

Lesions.—In two monkeys (*Macacus sinicus* and *Macacus rhesus*) we made a horizontal incision through the hemisphere in the plane of the anterior end of the intraparietal

[1] "Anatomie des centres nerveux," Tome 2, Fascic. 1, p. 145.

sulcus so as to cut off the fibres descending from the two central gyri. In a third animal (*Macacus rhesus*) we made a vertical stab incision beneath the whole length of the ascending parietal gyrus and continued beneath the two upper temporal gyri. In the two first cases fibres were traced to the thalamus opticus, but in one of them only could fibres be followed to the posterior brachium. In the third case, besides the fibres passing to the thalamus, others pass through the middle of the thalamus, some even entering the posterior commissure, while others were followed into the posterior brachium (probably temporo-mesencephalic fibres). A second group of fibres arise from the outer part of the crus and pass through the locus niger to ascend towards the tectum.

(*b*) Carnivora.—In three cats, one dog, and one badger, we made a strictly limited lesion in the post-crucial gyrus. In the one experiment on the dog we observed no fibres passing to the tectum (*cf.* Simpson *loc. cit.*), but this is only a single observation, and we do not therefore regard the question of their presence or absence in the dog as settled. In the cat and the badger a well-marked system of pallio-mesencephalic fibres exists. The fibres, for the most part large, leave the pyramidal tract in two definite groups, which we may speak of as upper and lower respectively.

The upper group of fibres, which are apparently those previously seen by Boyce, leave the internal capsule at about the junction of its outer and middle thirds, as seen in horizontal section; they pass backwards through the thalamus to the inner side of the corpus geniculatum internum, partly enter the anterior colliculus, and partly pass beneath it to the posterior colliculus; some of these fibres seem to terminate in the thalamus.

The lower group, which we think might conveniently be also called the cruro-tectal group, arise from the crus cerebri at points all along the outer one-third of its dorsal surface, and the more anterior of these pass inwards and terminate in the anterior colliculus and locus niger,[1] while the more

[1] Probably these are the fibres traced by Sherrington and others as connecting the crus and locus niger.

posterior pass upwards and backwards to gain the posterior colliculus. Many of these latter run in the inferior brachium. These fibres to the posterior colliculus terminate in the anterior half of the large ovoid nucleus of that body.

A few of the outermost fibres turn down from among those which pass beneath the superior colliculus and run in or with the tractus transversus peduncularis.

Combined Frontal and Parieto-Mesencephalic Fibres.

In four cats we separated the whole fronto-parietal region of the hemisphere by an incision which passed through the junction of the anterior and middle thirds of the hemisphere.

The effect of this large division of the corona radiata was to increase the number of degenerated pallio-mesencephalic fibres, as well as to cause degeneration of large numbers of fibres terminating in the thalamus opticus. These latter observations, therefore, are confirmatory of the fact that the so-called motor region is in close association with the anterior colliculus.

(4) *Fronto-Mesencephalic Fibres.*

To examine the important question whether the frontal region, *i.e.*, the area of cortex in front of the excitable cortex, sends any fibres to the mesencephalon we have made limited lesions of the frontal poles in two cats and frontal lobes in three monkeys. In the latter animal the posterior limit of the lesion was at least 4 mm. distant from the nearest point from which movement resulted on excitation. Although we obtained striking degeneration of the fronto-thalamic fibres (Dejerine), in these cases the only mesencephalic centre to which we could follow fibres was the upper (*i.e.*, anterior) part of the locus niger. No fibres, therefore, in our experience, go from the non-excitable part of the frontal lobe to the tectum.

A CASE OF ARRESTED DEVELOPMENT OF THE CEREBELLUM AND ITS PEDUNCLES WITH SPINA BIFIDA AND OTHER DEVELOP MENTAL PECULIARITIES IN THE CORD.

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II.—Naked-eye appearances of brain and cord.
III.—Histology of the brain.
IV.—Histology of the cord.
V.—Commentary.
Appendix:—Classification of cerebellar atrophies.

WE have been induced to place this case on record by the fact of its exhibiting what appears to be an undescribed combination of deformities of the nervous system, all of which seem to us to be of much interest from the developmental standpoint. One of us (W. B. W.) has made himself responsible for the examination of the brain, the other (K. W. M.) for the clinical history and the examination of the cord.

I.—CLINICAL HISTORY.

E. M. H., a female infant, aged six weeks, was brought to the Infirmary for Children, Liverpool, on August 10, 1901. Family history as follows:—A grandmother and aunt died of phthisis; the mother has one other child living; after marriage she had two miscarriages, then the eldest living child was born, then followed another miscarriage and then this child was born.

Anamnesis:—At birth a swelling was noticed at the lower part of the back; from this a creamy fluid was discharged for one day after birth; it grew larger and then gradually smaller after

the discharge had recommenced. The mother noticed that the head was enlarging at the third week. The child was born with club feet and without any use in the lower limbs ; she also had *prolapsus ani.*

On August 12 it was noted—there is a linear ulcer with a few granulations over the posterior aspect of the fourth and fifth lumbar vertebræ ; the spine is bifid here but there is no bulging. There is well-marked hydrocephalus. The eyes are prominent ; measurement from external auditory meatus to external occipital protuberance $10\frac{1}{8}$ in. The child shows no sign of being able to see but can hear. There is talipes equino-varus of the right foot ; the child moves the hands and arms freely but the legs are completely paralytic.

August 13.—Operation was undertaken to endeavour to drain the cerebro-spinal channels from the lumbar region. A flap was turned upwards exposing the second and third lumbar spines and laminæ, the latter cut and a tightly distended tube of membranes exposed ; this was closed below at the level of the fourth lumbar by cicatrix. This tube was opened and a bunch of horse-hair strands passed into the opening ; the other ends were carried laterally into a bed dissected up for them between the muscular layers and the peritoneum. The wound was entirely closed.

For the first four days this drainage appeared to act satisfactorily, but on the fifth there was a considerable amount of tension of the structures around the wound, so much so that it was necessary to remove the stitches; a slight amount of cerebro-spinal fluid came away into the dressings, but the drainage was much less satisfactory and the hydrocephalus persisted after showing at first some diminution. This condition of affairs continued until August 24, when the child showed signs of gastro-intestinal disorder, with vomiting and diarrhœa ; she died on the 29th. The temperature chart shows nothing calling for comment, except for a rise of temperature on the 24th, at the commencement of the attack of gastro-enteritis ; there was apyrexia throughout.

II.—Naked-Eye Appearances of Brain and Cord.

Post-mortem Examination (August 29).

The cranio-vertebral cavity was opened throughout its extent, In the lumbar region an unhealed wound marks the position of the operative procedure ; the arches of L. 4 and L. 5 are represented by stunted projections from the lateral aspect of each

body; the arches of L. 3 and L. 2 have been removed. At the level of L. 4 the meninges and contents pass into a dense mass of cicatrix; above this the dura mater appears unusually tough and thick throughout. At the level of D. 4, the whole of the structures in the canal, membranes and contents, are divided into two apparently equal halves, an exostosis proceeding from the centre of the posterior aspect of the body of the vertebra, passing backwards between the divided cord and membranes, and then curving to the right and becoming attached to the right lamina near its junction with the spinous process. To the naked-eye the spinal roots appear normal. Above and below the exostosis the cord and membranes are undivided.

On slitting up the dura mater of the cord, this latter structure is found to be embedded in a casing of loose friable material, from the lumbar region to the cervical, where it becomes gradually less marked. The appearance of the cord after dissection from this bed is seen in the photograph (Plate I). It is a delicate attenuated structure; below there is no cauda equina distinguishable, but the cord becomes involved in the cicatricial mass at the level of the spina bifida.

The upper extremity of the cord is marked off from the medulla oblongata by a V-shaped depression, terminating in the well-marked anterior fissure. There are no prominences corresponding to the anterior pyramid and olive, and the medulla passes insensibly into the pons, no trace of the thickening caused by the transverse fibres of the pons being visible; the median raphé is well-marked, and on each side of this, opposite the rudimentary cerebellum, a slightly elevated ridge is present. The crura-cerebri emerge from beneath the thickened upper extremity of the pons, attached to each other mesially for some distance before dividing to enter the hemispheres. The optic chiasma and tracts are of normal appearance, and the corpora albicantia well formed. On the posterior surface, faint longitudinal lines indicate the fasciculi of the cord at its upper extremity. The inferior peduncle is very poorly represented. The cerebellum is represented by a very rudimentary structure with a few leaflets; it is impossible in this to distinguish the various parts; the worm is represented by a small oval prominence. The superior peduncle consists of a delicate flattened band of tissue on either side. The mesencephalon is represented by a single large structure; no trace of a division into anterior and posterior corpora quadrigemina being seen; the optic thalami are of moderate size, and the soft commissure is well formed.

The cerebrum exhibits marked flattening of the convolutions and extreme dilatation of the lateral and third ventricles. With these exceptions the hemispheres exhibit no peculiarities.

After removal the brain and cord were immersed in Müller's fluid.

III.—Histology of the Cerebellum, Medulla, Pons, and Mesencephalon.

The series of figures accompanying this article shows that we had to deal with a case of defective development of the cerebellum and of all those parts of the central nervous system which are connected with that organ. It is on account of the complete nature of this agenesis and the manner in which it is chiefly confined to the cerebellum and its annexes, that the interest of the anatomical findings in these regions arises.

Cerebellum.—The extremely rudimentary character of this organ was found to be accompanied by a similar absence of histological development.

The figures given represent accurately the outlines of its convolutions, which it will be at once seen were of an extremely simple nature. In many places the organ was entirely unconvoluted, and represented by an undifferentiated mass of embryonic tissue and small cells.

It was impossible to recognise the various named lobes. The lateral parts of the organ seemed to be slightly better developed than the remaining part of the hemispheres, and here were found almost the only myelinated fibres present. In these regions also, in a few parts, a differentiation into a cortex with its three layers of granular and molecular strata and Purkinje's cells could be seen.

No trace could be found of central gray nuclei. It is to be especially mentioned that there was no evidence of sclerosis, or of vascular degeneration.

The bulb.—The well-defined column of Burdach could be traced into the corresponding nucleus, the cells of which were large and numerous. It is doubtful whether a nucleus gracilis could be distinguished; this nucleus commences normally at a lower level than the cuneate nucleus, and

is situated medially. The first cell mass to appear in tracing the posterior columns upwards was situated laterally, and evidently in connection with the fasciculus cuneatus. The condition of the cord, especially in the lumbar region, is to be regarded as the explanation of this appearance. From this nucleus internal arcuate fibres were seen streaming inwards, fairly numerous and well coloured by the Weigert stain. Their decussation and the upward continuation of the fillet were well seen. The pyramids and their decussation were also fairly well coloured, though not so markedly as the fillet system.

No trace of the inferior olives or of accessory olives was found. Their usual position was represented by a well-defined area of embryonic tissue, entirely devoid of medullated fibres or of cells having any resemblance to the cells of the olives (figs. 5 and 6). External arcuate fibres, both anterior and posterior, were absent. Nuclei arcuati could not be recognised.

The cerebellar peduncles.—The three peduncles of the cerebellum were practically absent. The restiform body begins in normal brains to be visible on the outer side of the superior extremity of the nucleus cuneatus, but this region was almost devoid of medullated fibres. In the pons, where it is situated between the two roots of the eighth nerve, there was found a scanty number of irregularly-arranged myelinated fibres.

Both the corpus restiforme proper and its inner part appear almost unrepresented; no vestibulo-cerebellar fibres can be traced, although, as will be stated later, the end nuclei of the vestibular nerve appear well developed. The absence of the major part of the inferior peduncle is, of course, to be considered as connected with the absence of the olives and the scanty development in the cord of the direct cerebellar tract and posterior columns.

The figures show that the transverse fibres of the pons and middle peduncles were almost entirely absent; a few sections showed a band of medullated tubes situated laterally, which apparently represented all that existed of these structures.

The pyramids were seen to be lying in a mass of embryonic tissue. No trace of pontal nuclei could be discovered.

It would appear also that the superior peduncle was absent, a condition to be expected, considering that the nucleus dentatus and nucleus ruber could not be found.

Perhaps a few fibres in fig. 12 are to be considered as belonging to that system, and in the mesencephalon there is a decussation corresponding chiefly to the fibres of Meynert and Forel, but which may in part represent the superior peduncle.

The nuclei of the cranial nerves and tegmentum.—The deep origins of the cranial nerves were readily seen, and the various cell groups seemed normal.

Especial interest centres in the eighth pair. The large ventral cochlear end nucleus is well formed, and the lateral fillet system normal. The superior olives and corpora trapezoidea are well coloured by the Weigert stain. Fibræ acousticæ are present, but not numerous.

With regard to the end nuclei of the vestibular nerve, so far as the method used will permit of observation, these cell groups were seen to be well represented, both by the central inner nucleus and the outer group of cells composing Deiters' nucleus. The various central and spinal fibres from these end nuclei could not however be recognised; in particular it was certain that no fibres passed into the cerebellum.

The posterior longitudinal bundle was well represented, but in the upper part of the pons, instead of occupying its usual position almost immediately beneath the fourth ventricle, it was seen to be separated from this by a mass of embryonic tissue (see fig. 11).

The nuclei tegmenti were fairly well seen.

Mesencephalon.—We have already mentioned the striking naked-eye appearance of this structure. On section the noticeable features were the entire absence of the red nuclei. The series of sections failed to reveal anything which resembled this important structure. The superior peduncles also were absent, with, perhaps, the exception of the rudimentary decussating fibres already alluded to. The feeble

development of the colliculi of corpora quadrigemina also arrested attention. In the pes the slight extent, laterally and medially, of the medullated tract, would appear to indicate that the *pars pyramidalis* only was represented—the fibres connecting the frontal and temporal lobes being absent. The third nucleus, fillet system, substantia nigra and fountain decussations were well seen.

IV.—Histology of the Cord and Membranes.

Cord.—The cord after fixation and hardening in Müller's fluid, was divided into twenty-four portions, each of which was embedded in paraffin. Sections from each were stained (*a*) by the Pal-Weigert method, after impregnation with Marchi's fluid ; (*b*) with hæmatoxylin and other chromatin stains.

The appearances found in sections from eight different levels will be described here, and any important points in intermediate sections also noted.

Series I. Upper Cervical (fig. 14).—The cord is reniform in shape. The central canal is represented by two channels ; in section each shows as a slit, one transverse, the other antero-posterior. The transverse channel is lined by columnar epithelium, but only over part of its wall ; the antero-posterior portion extends from within a few lines of the centre of the transverse towards the posterior margin of the cord ; it is unlined by epithelium but bound by a membrane ; between its anterior end and the transverse slit is neuroglial connective tissue. That these two portions each represent part of the canal is shown by the fact that they become continuous at a lower level. There is no trace of a posterior commissure. The gray matter shows numerous nerve-cells in the anterior horns, the medial, the anterior and the antero-lateral groups being well shown, the postero-lateral less so. The white commissure shows numerous medullated fibres. In the white matter medullated fibres are scanty throughout ; there is a well-marked postero-external tract, however, and in the anterior ground substance medullated fibres are also fairly numerous ; they are few and scattered in the direct cere-

bellar, antero-lateral ascending and descending tracts, and in the positions of the pyramidal tracts, and absent entirely in the position of the postero-internal column. In the latter locality and elsewhere, a fine neuroglial substance makes up that part of the cord outside the gray matter. The substantia gelatinosa is a very prominent structure.

Series II. Middle Cervical (fig. 15).—The canal is in the shape of a T, the vertical limb running towards the posterior aspect; the transverse slit is alone lined by columnar epithelium, and that in part only. In the gray matter the grouping of the cells is not distinct except that the mesial column is well marked; the cells of the lateral groups are numerous; the fibres of both anterior and posterior roots are distinctly medullated. Burdach's column is again well marked off, and contains numerous medullated fibres; the anterior ground substance also shows a considerable amount of medullation; but as before these fibres are few in the direct cerebellar, the pyramidal and the antero-lateral ascending and descending tracts, and absent entirely from the position of Goll's column. The medullated fibres in Burdach's column do not extend to the periphery of the cord. The substantia gelatinosa is as before a well-marked structure.

Series III. Lower Cervical. The Cord (fig. 16) is more flattened from before backwards than in the last series. This series is taken from the lowest cervical zone. The outline of the canal is in the form of a long transverse limb, and a short posterior extension from the centre of this. It is lined discontinuously with columnar epithelium; the apical part of the posterior limb is so lined, but not the remainder of this limb. The arrangement of the gray and white matter resembles that in the last series, that is to say, the postero-external column and the anterior ground substance are fairly well occupied, the remainder of the cord outside the gray matter being almost entirely without medullated fibres; in the gray matter the cells are numerous and well formed. By the lateral extension of the canal the anterior and posterior horns are cut off from one another. On the ventral aspect of the canal are a few medullated commissural fibres.

Series IV. Upper dorsal; just above the level of the division (fig. 17).—The cord is here a flattened ribbon-like structure, consisting of two lateral masses connected by a narrow strip. The canal extends from side to side across the middle line; on the one side it has a branched outline, on the other it is much smaller and spherical, the two lateral dilatations being joined by a slit with a narrow lumen; the epithelial lining is partial, the greater part being unlined. The gray matter is well represented on each side; in the anterior horns the mesial and lateral columns are large groups; by counting the cells of several sections it is found that the number is practically the same on each side. The only medullated fibres are a few in what appears to be the position of the postero-external column; the remainder of the cord structure is a fine gliosal tissue with numerous small cells.

Series V. At the level of D. 4; that is to say, at the division (fig. 18).—The halves of the divided cord are of about equal size, and irregularly circular in outline. The canal is represented on each side, but more extensively on one than on the other. On the left side the outline of the channel is oval, and it is completely lined by columnar epithelium; on the right side the outline is branched, and in some sections the branches appear as definite diverticula separated from the central channel by encroaching glial tissue. The cells in the anterior horns of each side are about equally divided in number; they are in two groups, one near the mesial, the other near the lateral margins of the horn. The amount of tissue outside the gray matter is now very scanty and staining with Pal-Weigert does not exhibit the presence of any medullation. The vascular spaces throughout the cord are large and numerous; that is to say, there appears to be unusual vascularity here.

Series VI. Lower dorsal; below the division (fig. 19).—The two halves have now reunited and form a cord of very diminished dimensions and reniform in shape. Here a remarkable change is met with, in that the central parts are disintegrated into a tissue of coarse fibrillar structure in which are numerous irregular cavities. This disintegration

has taken place posteriorly to the central canal, which is a transversely elongated slit. The outline of the canal is, however, largely obscured and the lumen invaded by the process of disorganisation. In addition to the coarse fibrillation of this disintegrated area, there are a large number of "colloid bodies" present throughout it, and also a few giant cells; fragments of columnar epithelium, evidently derived from the lining of the invaded central canal, are also found here and there; there is no round cell infiltration or any evidence that the process of change is of an inflammatory origin. There are a few well-formed ganglion cells in the anterior horn on each side. No trace of medullation in the fine gliosal tissue which constitutes the circumferential part of the cord.

Series VII. Mid-lumbar (figs. 20 and 21).—The cord is here reduced to very small dimensions; the kidney shape is noticeable. There are traces of the disintegrating process noted in the series above, but it is much less marked here; the sections show that this disorganisation, commencing at about D. 6 or D 7, reaches its maximum in the lower dorsal region, and disappears in the lumbar portion of the cord above the level of the spina bifida.

In this series there is no marked differentiation between gray matter and white matter; the whole structure is a fine gliosal tissue, the only exception being the presence of a few ganglion nerve-cells in the position of the anterior horns on each side. The outline of the central canal is slit-like from side to side, lined only in part by columnar epithelium.

Series VIII. Level of the spina bifida.—At this level the nervous tissue is represented by a central structure representing the cord, by nerves, nerve-roots and ganglia. All are embedded in a fine connective tissue containing numerous large vascular channels. The cord is more flattened than in the last series but is kidney shaped; there are a few nerve-cells in the position of the anterior horn on each side; no medullated fibres. The posterior ganglia exhibit numerous well-developed ganglion cells, but also show a marked hypertrophy of intercellular substance consisting of a highly cellular connective tissue.

Membranes.

Histologically the dura mater is of well-developed fibrous tissue. Within this the distinction of other coverings is entirely obscured by the material in which, as already described, the cord is embedded. This material consists of a highly cellular connective tissue containing numerous large thick-walled blood-vessels.

Ganglion Cells of the Cord.

Cervical region.—In this region there are three well-defined groups in the anterior horn. (*a*) Mesial column—large cells ten to fifteen in number. (*b*) Ventro-lateral column ten to twelve in number. (*c*) Dorso-lateral column, the largest of the three groups, seventeen to twenty cells. The numbers indicate the cells counted in each section and averaged.

Centrally to the dorso-lateral group are scattered cells of small size not marked off into groups but most numerous in the position of the middle cell column. No defined Clarke's column. No cells in posterior horn.

Upper dorsal region.—The cord here is elongated laterally. There are two well-defined groups of cells in the anterior horn. (*a*) Mesial group, large cells six to eight. (*b*) Lateral group not (subdivided) cells twenty-five to thirty in number. Between these groups but more centrally placed are a few scattered cells of small size five to seven in number. No cells in posterior horn.

Mid-dorsal region.—The total number of cells is smaller. The mesial and lateral groups are well defined and contain about an equal number of cells, twelve to eighteen in number, in different sections. There are also a few centrally situated, five to six in number. The cord is here divided. Immediately below the division—the mesial group is large—of large cells, fifteen to sixteen in number; the lateral group is composed of smaller cells, four to eight in number.

No cells outside these *two* groups.

Lower dorsal region.—The ganglion cells are, with the exception of a few scattered laterally, grouped into one mesial column, eight to ten in number.

Upper lumbar.—Cells very few in number; in some sections none are seen. The average is three in each anterior horn, placed antero-mesially.

Mid-lumbar.—The cells are here more numerous than in the upper lumbar region; they are in two groups, counted in eight sections at different levels :—

(1) Antero-mesial, 4, 3, 4, 2, 6, 1, 2, 4.

(2) Antero-lateral, 3, 1, 4, 3, 3, 5, 3, 2.

Sections of the posterior root ganglia show the cells to be numerous, large and well formed.

Summary.

A child aged six weeks, presenting a lumbar spina bifida ruptured at or before birth, and now healed; hydrocephalus; paraplegia of the lower limbs. Death from intercurrent gastro-enteritis.

(1) In the brain. Arrested development of the cerebellum and of its efferent and afferent fibres, and of their nuclei of origin; of the restiform bodies, the olives, accessory olives, external arcuate fibres and nuclei arcuati; middle peduncles and transverse fibres of the pons, pontal nuclei, vestibulo-cerebellar tracts; superior peduncles, gray nuclei of cerebellum, red nuclei of the tegmentum; possibly the cerebro-pontal cortical tracts.

(2) In the cord. General attenuation of this structure throughout, division at the level of the fourth dorsal vertebra into two equal halves; marked enlargement of the central canal which divides with the division of the cord; the presence of various irregular cavities in the cord and disintegration of its central parts in the lower dorsal region; normal development of the gray matter with well-formed ganglion cells; scanty development of white matter, its place being taken by tissue of neuroglial structure.

(3) The coverings of the cord. The whole cord, as far as the upper cervical area, embedded in a fine connective tissue with large vascular channels; the laminæ and spines of the fourth and fifth lumbar vertebræ deficient; an exostosis dividing the canal at the level of the fourth dorsal vertebra.

V.—Commentary.

The case exhibits a condition which may be generally described as arrested development of the central nervous system from the mesencephalon downwards, with a superadded local process of degeneration. In addition to this the abnormalities in the parts contiguous to the cord are to be considered, and on these we may first comment.

I.—The deficiency in the completion of the bony casing affects that section where the deformity is most commonly present. The exostosis which divides the canal and its contents is a rare developmental fault, but there are records of several cases presenting similar bony septa. Thus in the report of the Clinical Society on spina bifida four examples of this variation are recorded (1). One at the tenth dorsal vertebra, the whole of the laminæ and spines below being deficient; one in the lower dorsal region at the apex of a spina bifida involving the whole canal below, associated with an entirely bifid cord below; a third exhibiting a similar condition in the lumbar region, but with union of the cord below the exostosis; the fourth concerns a spina bifida of the last two dorsal and the upper two sacral vertebræ, the cord being divided into unequal parts and reuniting below.

M. Houël (2) has described a case in which a similar exostosis projected from the bodies of the third and fourth lumbar vertebræ, with its apex partially occluding the opening into the sac of a lumbo-sacral spina bifida; the cord at the point being divided into two parts and reuniting below. Sulzer (3) found in a lumbar spina bifida complete division with reunion below of the cord, apparently due to a similar exostosis.

It will be seen that these cases present one marked point of difference from that described here in that the exostosis and the division of the cord was in immediate relation with the deficiency in the vertebral arches constituting the spina bifida. M. Houël was of opinion that the exostosis in his case was in direct casual relationship with the deficient

laminar junction; on general grounds and in the light of this case it appears more reasonable to consider this variation in cases of spina bifida as merely concomitant, the deficiency in the laminæ and spines and the growth of such exostoses being all faults in the development of those groups of cells which form normally the bony casing of the cord. Another feature in which this case appears to differ from others similar is in the division of the meninges into two entirely separate tubes, each encasing one half of the cord. Apart from the presence of an exostosis such as was found in this case, the association of division of the cord and spina bifida has been recorded by several, *e.g.*, Recklinghausen (4), Koch (5), Ollivier (6). A division of the cord, a rachischisis, also occurs unassociated with spina bifida. A case of this kind is related by Recklinghausen (7), and another has been recorded by Foá (8). In each case, as in our own, the division was into two approximately symmetrical halves, with gray matter and white matter normally distributed, and with a central canal in each half. One of us (K. W. M.) has recently had the opportunity of dissecting a specimen which is also of interest in connection with this rachischisis. A fœtus born at full term exhibited a condition of anencephaly with spina bifida involving the cervical and dorsal regions. The nervous tissue representing the spinal cord was in the form of a tube with membranous wall, on opening which four prominent longitudinal ridges were seen to bulge into the lumen, arranged symmetrically, two on each side. These were found to consist of myelinated nerve-fibres; at the lower dorsal region the separation into two halves became distinct; on the right side the two ridges united to form a rounded cord, on the left the nervous tissue remained diffusely distributed on the inner surface of the membranous covering. The separation into right and left halves was complete but unsymmetrical.

This case and those of Recklinghausen and Foà, show that apart from the presence of a mechanical obstruction, a rachischisis occurs as a developmental fault, *sui generis;* in place of the union of the dorsal and ventral columns of nervous tissue on each side through the medium of the roof

and floor plates to enclose a single canal, each dorsal column unites with each ventral column and the floor and roof plates default. In the process of union of the dorsal with the ventral column, a portion of the lateral extension of the central canal is cut off, and in this way a channel is present in each half.

The presence of an exostosis, as in this case here recorded, affords an easy explanation of the etiology of the rachischisis; in the absence of such a condition the explanation of the division is not forthcoming; it is one of the rarest of deformities.

The tissue in which the cord was embedded is of much interest. At first sight it seemed probable that it was of the nature of an inflammatory effusion, but the histology entirely negatives this. The structure indicates an origin in mesoblast, in that portion of mesoblast which extends backwards in a double fold to enclose the neural tube, and which is spoken of by embryologists as the membranous primordial vertebral column, and from which the cutis, the vertebral arches and the cord coverings originate. As an erroneous developmental product it belongs to the same category as the maldevelopment of the vertebral arches. We are not aware of any quite similar observation recorded; Recklinghausen (9) has, however, placed on record a case of spina bifida occulta, in which a myofibrolipomatous tissue occupied the spinal canal in the lumbar region, and encircled the cord[1]; the structure in our own case is also analogous to that described by Mr. Bland Sutton (10) in the variety of spina bifida to which he gave the name myelocele. In this variety the medullary folds coalesce imperfectly, the central canal opens dorsally, and the tissue surrounding the furrow which is its continuation, shows microscopically nerve-cells, neuroglia and a few nerve-fibres embedded in a nævoid mass of dilated capillaries and connective tissue.

II.—Probably in the great majority of cases of spina bifida there exists also some developmental peculiarity in the cord. Even in cases of the uncommon simple menin-

[1] *Cf.* also Gowers' *Trans. Path. Soc.*, xxvii., 19.

gocele, the cord not unusually shows some abnormality; *e.g.*, in a case of apparently simple meningocele lately examined by one of us (K. W. M.), the cord exhibited a marked degree of hydromyelia above the level of the spina bifida.

The case now under consideration shows this involvement of the cord in an extreme degree. The central canal is not only of very large dimensions throughout, but its outline is similar, generally speaking, to that which is found in the embryo up to about the eighth week, at any rate in the cervical region of this case. The way in which the posterior limb of the canal is closed by the approximation of its lateral walls gives strong support to the belief that the posterior median septum (the so-called fissure) is normally formed by the growing together walls of the dorsal part of the canal. It is not easy to explain the deficiency of the lining of cylindrical epithelium over a considerable proportion of the wall of the canal; it appears necessary to attribute it to the increased area of the wall and the consequent proportionate deficiency of those cells which normally are sufficient to give the canal a complete lining. A similar deficiency has been noted by Chiari in cases of hydromyelia recorded by him (11). The ependyma is, however, a formed structure very early; the cells are ciliated in the human fœtus at the fifth week, and line the large canal, but this is, of course, of a much smaller surface area than the canal in the cord we are describing.

In the tissue of the cord itself the condition of first importance is that its substance is to a very large extent of a fine neuroglia structure, with marked defect in the development of the nervous elements proper. It must be remembered that the neuroglia is of epithelial origin, and derived from the cells of the neural tube; it is therefore the less specialised of the two elements which arise from these cells, and the development of the more specialised is at fault in this case. It is well known from the pathological anatomy of syringomyelia how frequently associated are abnormalities of the central canal and the presence of undeveloped embryonal nervous tissue of a fine neuroglial structure. The

presence of this glia tissue is differently explained; on the one hand it is widely held that in most cases the syringomyelia is secondary to an actual hyperplasia of glia tissue, a gliomatosis, an over-production; on the other hand a second view holds that the original starting point of the cavity formation is the presence of undeveloped glia tissue which should have been transformed, but which persists owing to the want of the normal guidance to transformation.

It seems clear that the preponderance of glia tissue in our own case is to be ascribed to checked development and arrested specialisation. v. Leyden (12), who holds that this glia tissue is a manifestation of developmental defect, recorded some years ago two cases of much interest for comparison with our own: one a child, aged two years, with syringomyelia enclosed by layers of embryonal glia tissue, and associated with encephalocele and a rudimentary cerebellum; the second case, a child aged two and a half years, with hydrocephalus, rudimentary cerebellum, and syringomyelia, accompanied by undeveloped embryonal glia tissue. Apart, however, from the distended central canal, we have in the lower dorsal region a localised area in which this embryonal tissue has undergone a definite degenerative process with resulting excavation of the central parts of the cord. Of the exact causation of this excavation we are unable to express a confident opinion. As before stated, there is no evidence which enables us to state that it occurred as a result of any actual inflammatory process strictly so called. The two most striking points in the histology are the presence of the "colloid bodies," and the occasional occurrence of a giant-cell system. The origin of these colloid bodies, which have been described in a variety of degenerative processes in the central nervous system, is variously interpreted. They are supposed by some to arise from myelin set free by the degeneration of the myelinated fibres, but this origin is out of the question here as there is no myelination in the region where they are found. The giant cell is, in our opinion, always a degeneration product, as a rule associated with the destruction wrought by a chronic inflammatory process, such as tuberculosis and

syphilis. On the whole we consider that the evidence is in favour of the incidence of an active disintegrating influence supervening on the congenital abnormality, and not of a simple degeneration from inherent or autonomous causes.

The case exhibits in a striking way the association of hydromyelus, gliosis, and true syringomyelia. It is known from the researches of His (13), Lenhossek (14), and others that the ependyma and neuroglia possess a common developmental origin; it is not surprising, therefore, to find abnormalities of the one associated with abnormalities of the other. Hoffman and Schlesinger have stated the dependence of the central gliosis, which is the basis of the majority of cases of syringomyelia, on a primary hydromyelia of the central canal; however this may be, the association is easily understood. As we have seen, in this case the central cells have provided but a partial lining for the canal, the remainder being lined by tissue of glia structure similar to that which constitutes the remainder of the cord outside. In relation to the genesis of syringomyelia the view is commonly held that a true hyperplasia of glial tissue is the first product, but authorities differ as to the question of referring this "gliosis" to a congenital abnormality. Hoffman says (15) "the basis and origin of the disease process is in most cases a congenital developmental anomaly, whereby nests of embryonal tissue remain behind the normal central canal; a plicated central canal possesses the same importance." Similarly Schlesinger: "I consider that the central gliosis originates in the central canal epithelium; with this are found for the most part other congenital anomalies, especially widening of the central canal; that the excavation of the new-formed tissue results from degeneration of the same, dependent on vascular abnormalities."

The case here before us does not conform to the most commonly observed type of syringomyelia in that there is no evidence of anything that can strictly be called gliosis or local proliferation of glia cells; but the whole cord shows a condition of gliosis, if this term means the presence of young glia tissue, and it is in this posterior to the central

canal that the degeneration and excavation is taking place. *It shows this cavity formation in progress, and its connection with an undoubtedly developmental anomaly.*

In Series IV. it is seen that on one side the canal has a branched outline, and that the branches tend to be cut off from one another by the encroachment of their walls; in this way also cavities partially or entirely lined by epithelium arise. It is doubtful whether persistent cavities in the cord result from such a process as this, as it appears probable that they will in the process of growth be encroached on to their obliteration.

The absence of myelinated fibres throughout the greater part of the cord is a matter which calls for remark. It is known that in cases of spina bifida where the cord is embedded in the sac wall, both it and the nerves originating from it exhibit an entire absence of medullated fibres. An example of this peculiarity is reported by the Clinical Society's Committee.

In our own case the number of myelinated fibres is very scanty throughout the whole cord, and they are chiefly absent from the system tracts throughout. These fibres are present only in (*a*) the anterior and posterior roots, and (*b*) the postero-external column, and the ground fibres of the antero-lateral region, that is to say in the ground tracts above the division of the cord. It is in these regions that the fibres normally first acquire their medullary sheaths, and the arrested development of this case confirms in this way the information which has been derived from the study of the natural process.

III.—A considerable number of cases of atrophy of cerebellum have been recorded since Combette's often quoted paper in 1831. Many of the earlier cases were not examined microscopically, or only by the older, obsolete methods, and hence do not possess much anatomical interest. In the last ten years however, several detailed and valuable accounts of this condition have appeared, notably the papers by Menzel, Max Arndt, Spiller, Thomas and Dejerine (*vide* Appendix). These writers also give a fairly complete account of the literature, especially is this so in the detailed analyses

given by Thomas in his "Thesis on Le Curvelet." Ferrier also in "Allbutt's System" tabulates the cases since 1879, correlating the clinical symptoms with the anatomical findings. He thus completed the list given by Nothnagel in his "Tophische Diagnostik."

Lastly, quite recently Dejerine and Thomas have given an account of a case with an unusual pathogenesis. The origin of these conditions, indeed, varies very greatly, and in an appendix we have endeavoured to classify the cases on a basis on what appears to be their mode of origin. The clinical interest of many of the cases is considerable, first because they show the symptoms resulting from simple defect of this organ, and secondly, because of the increased interest which these observations have thrown on the nature of the hereditary ataxia of Marie, Friedreich's disease, and certain allied conditions. The clinical aspect of the subject does not now concern us, but we may mention one fact which appears to be very clearly illustrated by a study of the cases, viz., the same symptom group may appear with very different anatomical lesions. Thus, the cases of Nonne and Muira showed a simple smallness of the cerebellum. Spiller's is one of sclerotic atrophy, Menzel's of sclerotic atrophy with lesions of the cord, and Meyer found that the cord alone was affected, yet in all these cases the symptoms were closely allied.

The interest in the present case is for the most part anatomical; in the brain at least the condition appears to be one simply of arrested development, and owing to its completeness the relationship which exists between the cerebellum and its annexes is demonstrated in its main features with remarkable clearness, and confirms if it does not add anything new to our knowledge on this subject.

As to the date at which the development became defective it is difficult to say; it must have been very early, for the olives can normally be made out at the end of the third month. The growth of the organ must, however, have been irregular, for Purkinje's cells, which were found to some extent, usually only appear about the sixth month, whilst the corpus dentatum, which also, according to Obersteiner, appears at that time, was absent.

The majority of anatomical findings which we hope will be obvious from a consideration of the figures and the text, do not require any comment, they contain what is established both by a study of similar cases and by various other methods of research.

A few points merely may be mentioned.

The absence of external arcuate fibres, combined with the integrity in part at least of the dorsal column nuclei, has been noticed by a good many observers, as in the cases of Menzel, Arndt, Cramer, Thomas, and Spiller. In these cases the nuclei arcuate were also absent, and the fact suggests, as Bechterew supposes, that these cells form relay nuclei. Menzel believes some of these fibres arise in the cerebellum.

So far as the method employed permitted, no atrophy was noted in the nuclei reticularis tegmenti; the cells appeared numerous and large. This is important in view of the finding of Cramer in his case of unilateral atrophy, that the nucleus on the contra-lateral side was atrophied. Cramer contends that his case shows the connection of this nucleus with the middle peduncle.

The fasciculus centralis tegmenti is described by Bechterew and Flechsig (*Neurolog. Centralb.*, 1885) as a descending tract terminating in the olive and forming by this body a connection between the lenticular nucleus and cerebellum. It is situated just external to the inferior olive, and higher up between the superior olive and fillet. Spiller believes it was atrophied in his case, and in ours also it cannot be seen. Short tegmental fibres appear numerous and well stained. It is also of interest to note that the fillet and posterior longitudinal bundle were both well developed, notwithstanding the absence of the olive and cerebellum. This is in accord with the experimental results of Ferrier and Turner.

Lastly, we have mentioned that there is some reason to regard the fronto- and occipito-temporal frontal tracts as being undeveloped. This is difficult of explanation, as it is generally regarded that both are corticofugal systems. It may be mentioned, however, that Obersteiner, in the last edition of his "Anatomy of the Nervous System," states that the latter tract is in part corticopetal.

In conclusion, we wish to direct attention to the history of the pregnancies of the mother of this child—two miscarriages after marriage, then a living child, then another miscarriage, followed by the child here described. Such a history suggests syphilis, but no further evidence could be obtained in support of this suggestion. If syphilis was concerned in this case, and we believe that the history of many cases of spina bifida is tainted by this disease, its activity produced a series of remarkable defects in the fœtus.

References.

(1) *Clin. Soc. Trans.*, vol. xviii., p. 357.
(2) *Bull. et Mem. de la Soc. de Chir.*, May 9, 1877.
(3) *Ziegler's Beiträge*, xii., 4, p. 566.
(4) *Virch. Archiv.*, Bd. 105, p. 413.
(5) *Beitr. z. Lehre v. d. Spina Bifida*, 1881.
(6) *Traite d. Malad. d. l. Mœlle épiv.*
(7) *Loc. cit.*, p. 409.
(8) *Riv. sperim d. Freniatia*, 1878.
(9) *Loc. cit.*, p. 243.
(10) *Lancet*, 1888, vol. i., p. 359.
(11) *Denkschr. d. Wein. Akad.*, Bd. 63, 1895.
(12) *Virch. Archiv.*, Bd. 68, p. 1.
(13) *Arch. f. Anat. u. Phys.*, 1890.
(14) *Der feinere Band. Nervensystems*, Auf. ii., p. 176.
(15) *Deut. Zeitschr. f. Nervenheilk.*, Bd. iii., p. 82.
(16) *Die Syringomyelie*, 1895, p. 188.

APPENDIX.

A Classification of Cerebellar Atrophies arranged on the Basis of their Probable Pathogenesis.

I.—Cerebellum almost completely absent on one or both sides. Condition primarily due to arrest of development.

1. Combette.—*Bull. de la Soc. Anat.*, 1831.

   An epileptic idiot died, aged 11. A gelatinous membrane which represented the cerebellum was connected with the medulla by two membranous peduncles. Pons absent. Cord and brain normal.

2. D'Andral.—*Clinique Médicale*, vol. v. (abstract from Thomas, *Le Cervelet*).

   A woman died, aged 45. Mentally feeble and liable to incoordinated movements in the limbs. Left cerebellar hemisphere practically absent.

3. LALLEMENT.—*Soc. Anatomique*, 1862.

Patient died from apoplexy, aged 53. No symptoms during life. The left cerebellar hemisphere was absent with the same sided superior peduncle and contra-lateral olive and nucleus ruber tegmenti.

4. LEYDEN.—*Virchow's Archiv.*, lxviii., 1876.

Two infants with meningocele, syringomyelia and absence of cerebellum.

5. HITZIG.—*Archiv. f. Psychiatrie*, xv., p. 267, 1884.

Patient died, aged 33. As a child was of slow intellect, gradually developed symptoms resembling general paralysis, with ataxia of both extremities and oscillation of the body.

Right cerebellar hemisphere reduced to a minimum, middle peduncle and pons with contra-lateral olive absent.

6. FERRIER.—"Functions of the Brain," 1886.

Girl died, aged 15. Mentally feeble, with general muscular weakness and tremors of the hands.

The cerebellum was represented by a minute nodule. Pons and peduncles were absent.

7. NEUBURGER AND EDINGER.—*Berlin Klin. Wochen.*, 1898.

Man died, aged 46. He presented no nervous symptoms but suffered from bradycardia, death from cardiac failure.

Right cerebellar hemisphere practically absent.

Diminution of right superior and middle peduncles with the contra-lateral olive and red nucleus. Diminution in the central gray cerebellar masses and in the left nuclei pontis.

8. This case 1902.

II.—Cerebellum congenitally small, but of normal histological structure.

1. OTTO.—*Archiv. f. Psych.*, p. 730, 1874.

Man died, aged 39. Mentally feeble, but no physical inability.

Cerebellum was very small, pons rather narrow, but brain and cord normal in size.

2. VERDELLI.—*Rivista Clinica*, 1874 (abstracted from Thomas).

Man died, aged 19. Markedly rachitic. Epileptic convulsions from two years old.

Proportional reduction in size of cerebellum, medulla, and pons.

3. NONNE.—*Arch. f. Psych.*, 1891.

Patient died, aged 40. This is one of the cases in which Marie founded his "Hereditary Cerebellar Ataxia." The whole central nervous system was small, but especially the cerebellum.

4. MIURA.—*Mittheil. der med. Fac. der Kaiserlich*, Japan univ. *La Tokio*, Bd. iv., Heft 1, 1898. "Abstract from Dejerine and Thomas" (*loc. cit.*).

   One of two brothers exhibited symptoms similar to those in Nonne's case. Smallness of the whole central nervous system, especially of the cerebellum.

5. FRASER.—*Glasgow Med. Journal*, 1880.

   Another case with symptoms resembling those associated together by Marie. Pathologically the examination was incomplete, but smallness of the cerebellum was the chief lesion with slight histological defects in its structure.

III.—Comprises the majority of cases. There is an atrophy with a general sclerotic condition. The cortex appears primarily affected, either the whole or in part. The disappearance of the white matter corresponds to the extent of cortical defect. There are often indications of chronic meningitis and vascular degeneration. The symptoms are often those of epilepsy with mental enfeeblement, and in a number of cases date from the occurrence of some acute infectious disease in early childhood. It is difficult to discern the exact pathogenesis of these conditions, probably an acute disease acts as an exciting agent in developing a previously existing morbid condition, and leading to retrograde changes in nervous tissue.

The vascular changes are in this division of cases usually secondary in great part.

1. DUGUET.—*Soc. Anatomique*, 1862 (abstracted from Thomas).

   (α) Woman died, aged 39. No symptoms till 26, then epileptic fits and general weakness developed.

   (β) Man, aged 72. No symptoms till three months before death, then convulsions occurred, followed by incoordination movements.

   (γ) Patient died, aged 17. Epilepsy since 18 months old.

2. MAYNERT.—*Wien. Med. Jahr.*, 1864.

   Died aged 62, from mitral disease. Symptoms began three years before death. They were incoordination, trembling, and affection of speech.

3. CLAPTON.—*Trans. Path. Soc.*, London, 1871.

   Died at 33 from pleurisy. Measles at 4 years old, and then gradually unsteadiness in walking, enfeeblement of intellect, and inability to properly use his hands.

4 PIERRET.—*Archiv. de Phys.*, 1872.

   Died aged 69. At 4 had a "fit," and never quite recovered. Staggering gait developed.

   Cerebellum, middle peduncle and olives markedly atrophied.

5. MESCHÈVE.—*Virchow's Archiv.*, p. 559, 1880.

Died aged 40. Epilepsy with mental alteration, rotation in direction of an entering corkscrew. Gait oscillating, speech scanning.

Sclerosis of right cerebellar hemisphere and nucleus dentatus.

6. CLAUS.—*Arch. f. Psych.*, vol. xii., p. 669, 1882.

An insane epileptic.

Partial sclerosis of cerebrum and cerebellum.

7. KIRCHOFF (Case II.).—*Arch. f. Psych.*, Bd. xii., 1882.

Woman of 20 died from phthisis. There was trembling and slow choreiform movements.

Cerebellum was very small and hard. K. believes a sclerotic process had become engrafted to an arrest of development occurring at the seventh month.

8. BORRELL.—*Neur. Centralb.*, 1883.

Died aged 38. Convulsions and mental defect since infancy, tottering gait, tonic spasm of the muscles of the neck. Pia mater thickened.

Left cerebral hemisphere practically absent, right much diminished. Olives invisible and pons very small.

9. MAYOR.—*Journal of Mental Science*, 1883.

Died aged 32. Epilepsy and idiocy since birth. No disorder of movement.

Right cerebellar hemisphere sclerosed, with some healthy patches in places.

10. SOMMER.—*Neur. Centralb.*, 1884.

Died aged 30. Severe cerebral illness at 3 years old; in the latter period of life was subject to psychical agitation, and a peculiar gait of propulsion and staggering.

11. INGELS.—*Bull. de la Soc. de Med. de Belgique*, 1884.

A dangerous epileptic. No motor disorder.

Pons as well as cerebellum atrophied.

12. BOURSONT.—*Annal. Medico-Psych.*, 1891 (quoted by Thomas).

Four cases of insane persons with atrophy of cerebellum.

13. MENZEL, 1891.—*Archiv. f. Psych.*, 1891.

Illness began at 34. Ataxia of all limbs, increased knee-jerks. Tetanic-like contraction of muscles of neck. Affection of speech.

Cerebellum very small, absent in parts altogether. Both cortex and white matter markedly affected. Atrophy of pons and pontal nuclei, olives, part of restiform body. In the cord the posterior columns, pyramids, and dorsal cerebellar tract were found diminished in size. Menzel regards the case as one of primary development error, and the spinal lesion as due to a chronic meningitis. No evidence of vascular disease or of increased connective tissue formation.

14. HAMMARBERG.—*Neur. Centralb.*, 1892.

Died aged 24. At 7 years old severe "cerebral inflammation," gradually followed by oscillatory movements and staggering gait.

Both hemispheres the seat of a sclerosis especially attacking the cortex, also patches of sclerosis in the frontal lobe and in left olive.

15. CRAMER.—*Beiträge z. Path. Anat.*, Bd. xi., p. 39, 1892.

Died aged 48. Epileptic since 14, with mental alienation. No particular motor disorders.

Left cerebellar hemisphere sclerosed and atrophied.

16. ROYET AND COLLET, 1893.—*Archiv. de Neurologie*, 1893.

Death at 56. Appears to have been well up to age of 48, then developed staggering gait, increased knee-jerks, slight tremors and nystagmus.

Cerebellum hard and sclerosed, with atrophy of the middle peduncle and pons. No microscopic examination.

17. MOELI.—*Neur. Centralb.*, p. 553, 1889.

18. BOND.—*Journal of Mental Science*, p. 409, 1895.

Died aged 60. Mental deficiency since 17.

Ataxia and general tremor. Symmetrical atrophy and sclerosis of all parts of cerebellum.

19. SPILLER.—*Brain*, 1896.

At 5 years of age scarlet fever and diphtheria, and since then trouble in walking, gait staggering, mental deficiency. Died at 19 from tuberculosis. A sister affected in the same manner.

Post mortem.—Deficiency of corpus callosum, small size of cerebellum, atrophy of left cerebral hemisphere. Sclerosed areas in the cerebellum with thickened vessels. Atrophy of inferior olives, middle peduncle of pons, and pontal nuclei. External arcuate fibres and nuclei arcuati and diminution of nuclei reticularis tegmenti.

IV.—Primary vascular disease, attended by chronic interstitial inflammatory changes, chiefly affecting the white matter. Comparable to cirrhosis of the kidney.

1. SCHUTZE, 1887.—*Virchow's Archiv.*, 1887.

Death at 43. Diabetes insipidus since infancy. Developed a staggering gait, slow speech, traces of the intentional tremor, gradual paralysis.

Endareritis obliterans of basilar and vertebral arteries. Cerebellum greatly atrophied from a patchy sclerosis, molecular and granular layers little affected, Purkinje's cells showed marked changes. Increase in neuroglia tissue and diseased vessels. White matter greatly destroyed. Dentate nucleus and superior peduncle, olives and middle peduncle were markedly atrophied. Cord normal.

2 Max Arndt, 1894.—*Archiv. de Psychiatrie*, 1894.

Death at 70. Symptoms for the last four years. Gait unsteady, ataxic movements with paresis in arms and legs.

Thickening and disease of arteries at base of brain, cerebellar sclerosis, evidence of chronic inflammatory changes in its substance, dilated capillaries, round-cell infiltration, thickened fibrous tissue. In the cortex Purkinje's cells mostly affected, the molecular and granular layers practically normal. The white matter markedly sclerosed, atrophy of middle peduncle and transverse fibres of pons, of olives. Integrity of the nuclei of posterior columns of cord, but some atrophy of fibræ arcuatæ, internæ and externæ.

V.—A primary atrophy affecting the cerebellar cortex, the nuclei of the pons and the inferior olives, accompanied by marked atrophy of the middle peduncle and partial atrophy of the restiform body. No increase of connective tissue or of altered vessels. This atrophy of cells is considered to be comparable to the Duchenne-Aran atrophy of the cells in the ventral cornua.

1. Thomas, obs. iv.—*Le Cervelet*, Paris, 1897.

Patient died, aged 62. Symptoms began at 55. Staggering gait, oscillation of the body, scanning speech.

Cerebellar cortex greatly diminished in all its component parts. Gray nuclei intact. In the cerebellar medulla there was distinct diminution of myelinated fibræ. Atrophy of transverse fibres of pons. Middle peduncle, outer part of corpora restiforma, inferior olives, nuclei arciformi and superior external arcuate fibres.

2. Thomas, obs. v.

Age 44 at death. Illness began at 25, with progressive enfeeblement of lower limbs, later, mental incapacity, paresis, tremors, universal loss of sensation of all form.

Cerebellar cortex markedly atrophied while white matter only slightly affected. Atrophy of olives, middle peduncle, tranverse fibres of pons, restiform bodies (partially), cells of nuclei of Goll and Burdach, internal and external arcuate fibres. In the cord the posterior and dorsal and ventral cerebellar tracts affected.

3. Dejerine and Thomas (two cases).—*Nouvelle Iconog de la Salpet.*, 1900.

Case (1).—Death aged 55. Illness began about 3 years earlier, gradual inability to walk owing to trembling and staggering, speech become scanning in character. No loss of power or of muscle sense, knee-jerks increased.

Atrophy of cerebellar cortex with degeneration and disappearance of afferent and efferent fibres, of olives, and pontal nuclei, while the central gray nuclei were intact with the superior peduncle and nucleus ruber tegmenti.

Case (2).—Clinical history only given.

Description of Figures.

Figs. 1 to 13.—*A series of transverse sections from the upper cervical region to the superior extremity of the mesencephalon. Drawn by means of Edinger's drawing apparatus.*

Figs. 1 and 2. Show commencement of pyramidal decussation. Note the scanty peripheral fibres and the entire absence of fibres in the internal dorsal region of the cord. In fig. 2 the nucleus cuneatus is just becoming visible.

Fig. 3. Pyramid has almost crossed.

Fig. 4. Section at level of fillet decussation.

Fig. 5. Level of usual site of inferior olive, here represented by embryonic tissue. Note scanty peripheral fibres representing the spinal cerebellar tracts.

Fig. 6. Upper level of inferior olive, commencement of vestibular root and rudimentary corpus restiforme.

Fig. 7. Commencement of lateral fillet system, the anterior region of pons entirely devoid of nerve-fibres.

Fig. 8. Level of sixth and seventh nerves.

Fig. 9. Section of maximum development of the cerebellum.

Fig. 10. Level of fifth nerve. Note absence of transverse fibres in pons, possibly the medullated tract situated laterally is a representative of these.

Fig. 11. Upper level of pons.

Fig. 12. Lower part of mesencephalon. Note limited area occupied by medullated fibres in the pes. Well-marked fibres of Meynert and Forel, and perhaps also some representative of the superior cerebellar peduncle.

Fig. 13. Level of third nucleus. No nucleus ruber tegmenti seen.

Figs. 14 to 21. A series of transverse sections from the upper cervical region to the upper lumbar, described in the text.

Abbreviations.

pyr. = pyramid.
s.g. = substantia gelatinosa.
n.c. = nucleus cuneatus.
dec. fil. = decussation of the fillet.
des. rt. v. = descending root of fifth cranial nerve.
cor. rest. = corpus restiforme.
cor. trap. = corpus trapezoideum.
s. ol. = sup. olive.
n. coch. = Cochlear nucleus.
n.d. = Deiters' nucleus.
n.c.v. = nucleus centralis vestibularis.
p.l.b. = posterior longitudinal bundle.
n. v. = fifth nucleus.
s. ng. = substantia nigra.
dec. M. & F. = decussation of Meynert and Forel.
a.r.f. = anterior root fibres.
ant. horn = anterior horn.
g.c. = Goll's column.
post. r. = posterior root.
c.c. = central canal.
a.g.s. = anterior ground substance.
a.f. = anterior fissure.
ar. deg. = area of degeneration.

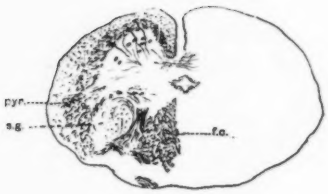


FIG. 1.

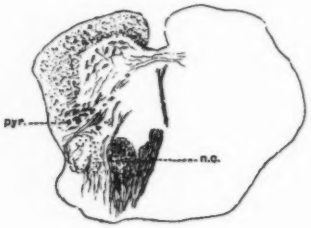


FIG. 2.

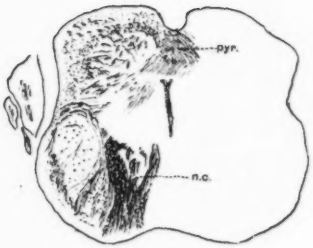
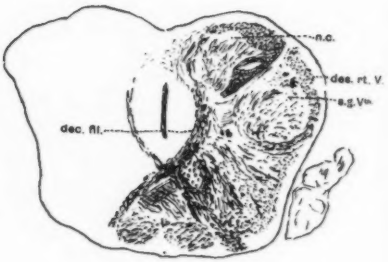


FIG. 3.



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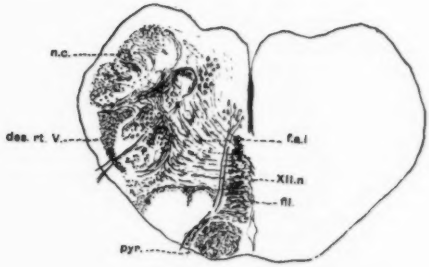

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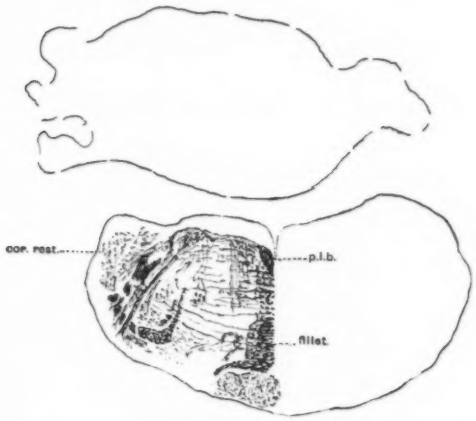

cor. rest.
p.l.b.
fillet

FIG. 6.

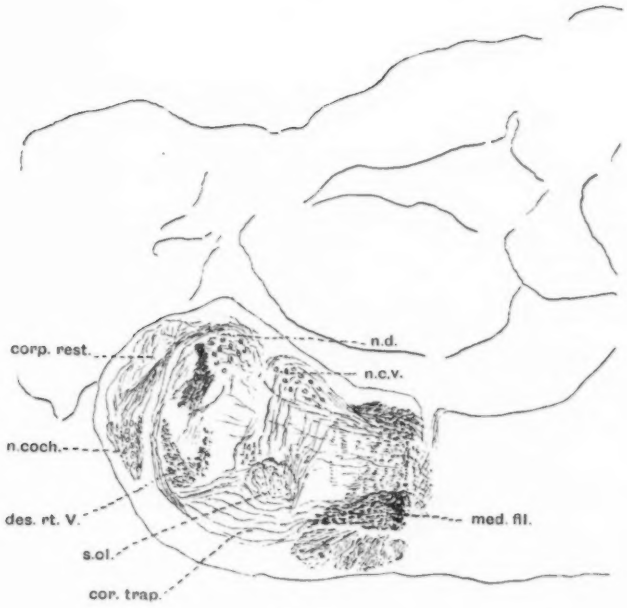

corp. rest.
n.d.
n.c.v.
n.coch.
des. rt. V.
med. fil.
s.ol.
cor. trap.

FIG. 7.

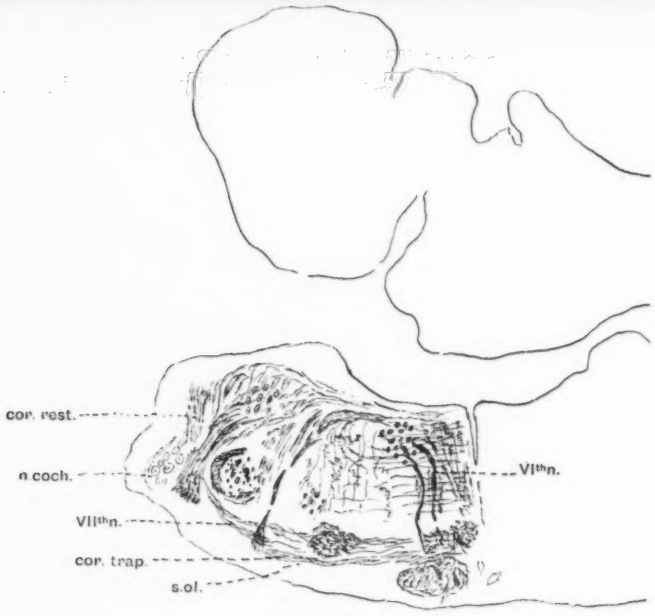

cor. rest.
n coch.
VII^th n.
cor. trap.
s.ol.
VI^th n.

FIG. 8.

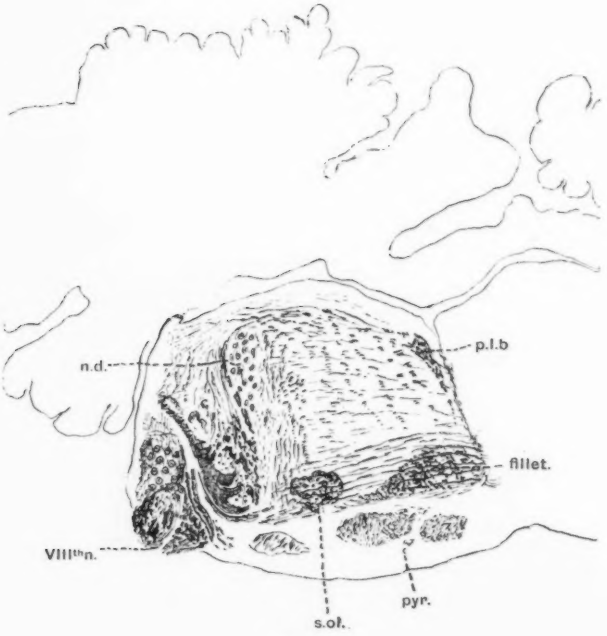

n.d.
p.l.b
fillet.
VIII^th n.
s.ol.
pyr.

FIG. 9.

n. V.
p.l.b.
pyr.

FIG. 10.

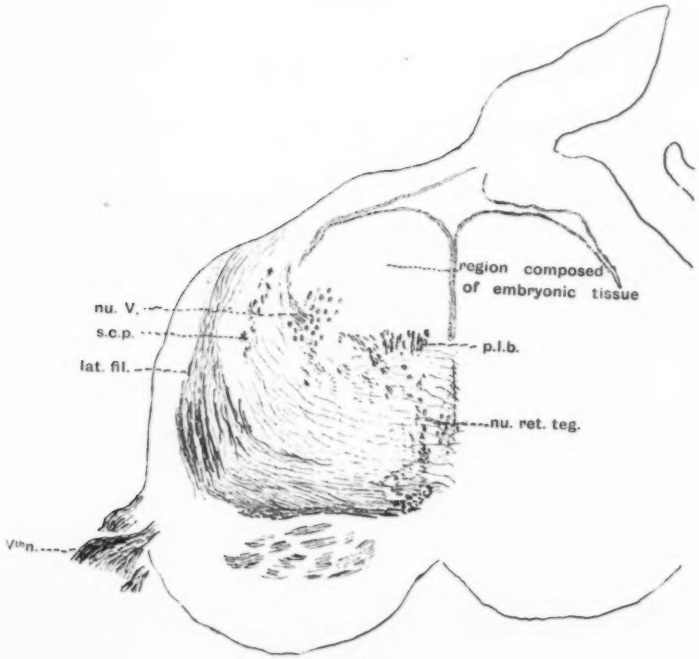
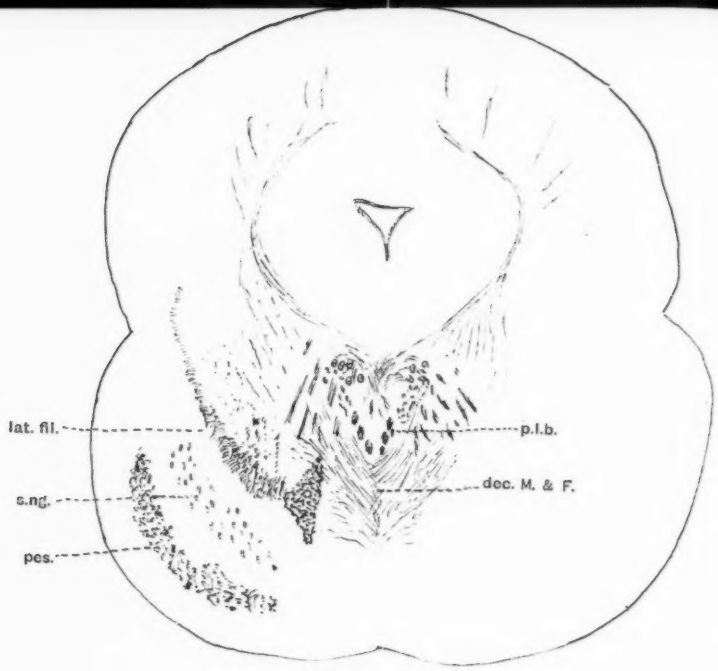

region composed of embryonic tissue
nu. V.
s.c.p.
lat. fil.
p.l.b.
nu. ret. teg.
Vth n.

FIG. 11.



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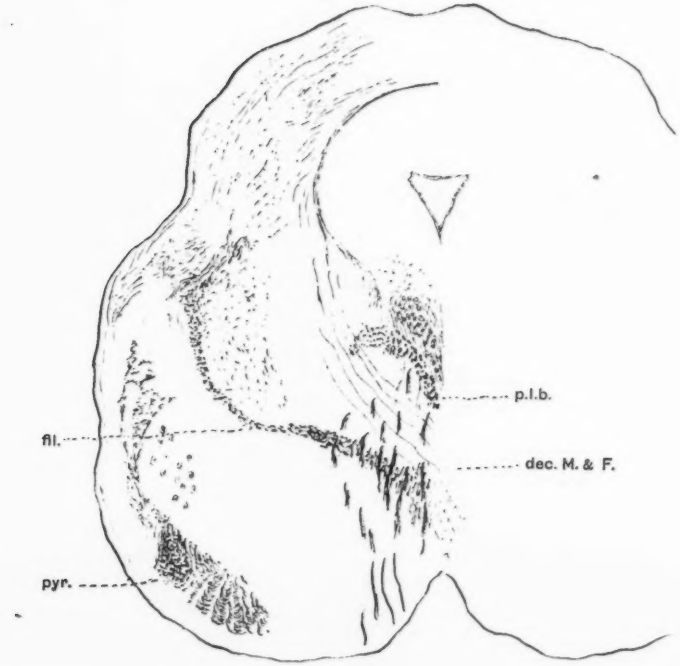

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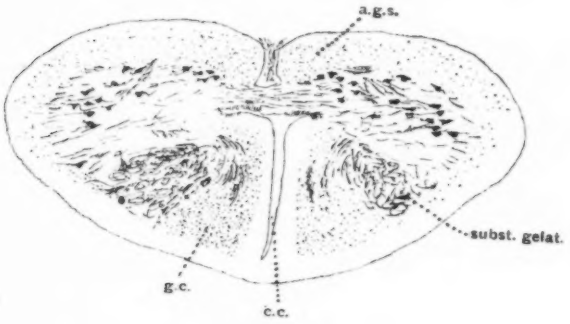

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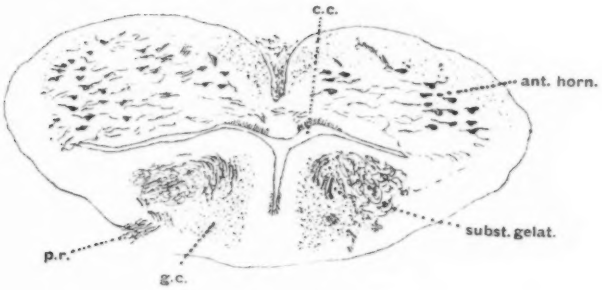
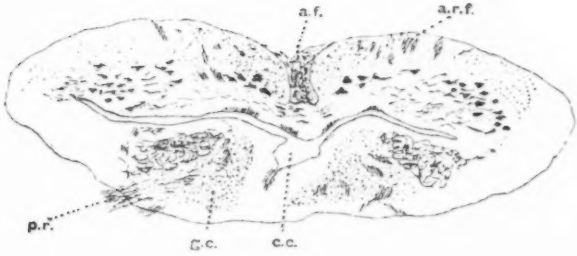


FIG. 15.



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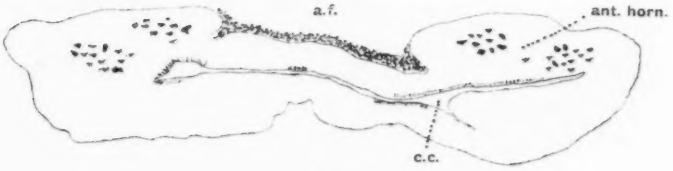


FIG. 17.

FIG. 18.

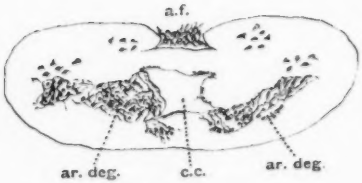


FIG. 19.

FIG. 20.

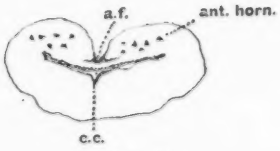
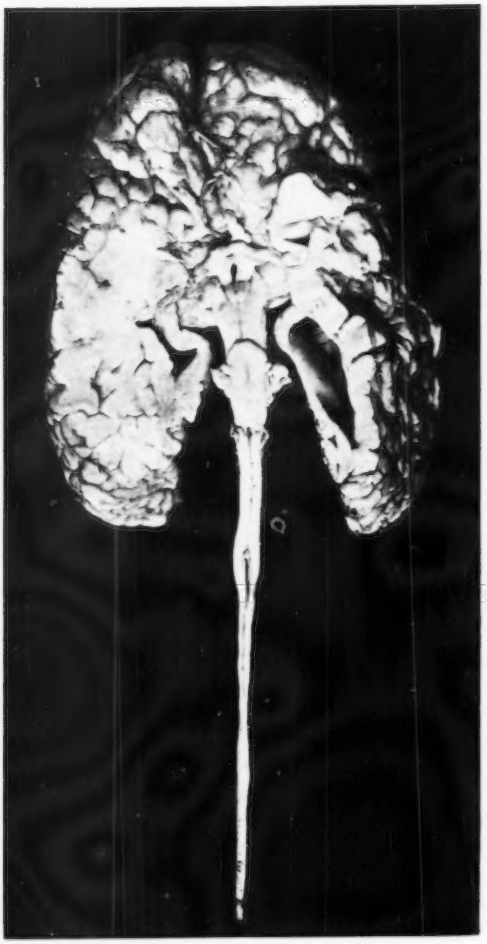


FIG. 21.

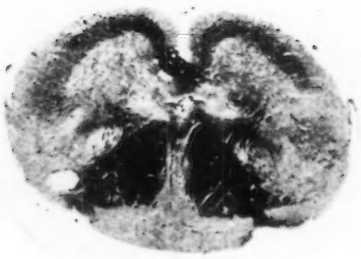
PLATE I.



Anterior view of brain and spinal cord.

To face page 478.

PLATE II.



Photograph at the level of second cervical segment.

To follow Plate I.

TOXIC DEGENERATION OF THE LOWER NEURONES SIMULATING PERIPHERAL NEURITIS.

BY STANLEY BARNES, M.D., B.Sc., M.R.C.P.,
Senior House Physician to the National Hospital for the Paralysed and Epileptic, Queen Square.

THE cases recorded in this paper present a clinical picture similar in many respects to what is met with in peripheral neuritis, and yet in other ways resembling progressive muscular atrophy. I have been able to collect together seven instances[1] of this condition which have recently come under observation at the National Hospital, and I am indebted to Dr. Buzzard, Dr. Bastian, Sir William Gowers, and Dr. Ferrier, for their kind permission to publish these cases.

Case 1.—Lizzie B., a domestic servant, aged 21, was admitted to the National Hospital, Queen Square, on December 18, 1892, complaining of difficulty in walking and weakness of the hands for three and a half years. The family history was unimportant. Although she said she had always been a delicate child, her only previous illnesses had been measles in childhood, and anæmia since the age of 14; the latter had persisted with varying severity up to the onset of the present illness.

In the spring of 1899 she was in bed for a fortnight with rheumatic fever; the attack was a slight one, and in a few days she was about again doing light house work. A week after getting about, she found that the right hand was beginning to get weak, and that the fingers would go blue and cold. The weakness slowly increased, and shortly afterwards began to appear in the left hand, whilst her walking also became impaired. By June, 1899, she had to give up her work, and by July, 1899, the weakness had become so great that she was obliged to take to her bed. The weakness still increased, and for four or five weeks (August, 1899) she lay in bed unable to feed herself, with difficulty in

[1] Whilst this communication was in the press, Case 3 died in hospital; the results of the autopsy are reported in the appendix to this paper.

swallowing and in speaking. Bed-sores and incontinence of urine and fæces came on, and a hectic temperature was recorded; delirium was present at times. From this point forwards (September, 1899) she began steadily to improve. She recovered control over her sphincters, swallowing and speech became natural and the bedsores healed. By May, 1900, she had sufficiently recovered to be able to walk with assistance, and to feed herself; since then she has slowly but steadily improved. Whilst at her worst the limbs were absolutely helpless, and very tender, although quite numb; the subjective sensory signs had been absent for about a year before coming into hospital.

On admission she was a fairly well-built healthy looking girl, with no sign of visceral disease. Her memory was good and she was not emotional. There was no impairment of function of any of the cranial nerves, and the pupils reacted well to light. The muscles as a whole were well developed, especially the trunk and proximal limb muscles. In the arms the extensors and flexors of the elbows were of fair strength, but the extensors of the wrist were markedly weak and atrophic; the flexors of the wrist were also weak, but not so weak as the extensors. Most marked, however, was the great atrophy and weakness of the small hand muscles, especially on the right side; the thenar and hypothenar eminences had almost disappeared, and no faradic or galvanic excitability could be obtained here or in the lumbricales or interossei. The hands adopted the *main en griffe* position, but this could easily be reduced on manipulation.

In the lower extremities, the small muscles of the feet and the anterior tibial muscles were considerably atrophied and almost powerless; no reaction to faradism could be obtained in either set of muscles; the calf muscles were of only moderate power, not nearly so strong as they should have been in a girl of her build; the extensors and flexors of the knee were stronger but probably deficient, whilst hip movements were well performed. The weakness was almost completely symmetrical in both upper and lower extremities, but in both the right limbs tended to be more severely affected.

Slight tenderness of the calves on pressure was the only sensory sign present. Both feet were purplish-blue in colour and were usually very cold; the toe-nails were ribbed and atrophic (since the illness). The skin over the fingers was glossy and smooth, and usually moist with perspiration.

The jerks in the arms were normal; the knee-jerks were present, but diminished; the ankle-jerks were absent on both

sides, and the plantar reflexes were difficult to obtain, but of the flexor type. Romberg's sign was absent. The gait was of the "dropped foot" type, without any ataxia.

There was a slight bluish line on the gums opposite several teeth, and of the kind usually seen in cases of lead poisoning; but no history of any lead poisoning could be obtained, nor had she ever suffered from colic. Alcoholism and diphtheria were also definitely excluded.

Under treatment she slowly improved, the forearms and legs especially recovering; the hand and foot muscles showed only slight recovery after a five months' course of massage and galvanism.

Case 2.—Emily G., a single woman, aged 28, was admitted to the National Hospital on August 10, 1900, complaining of weakness of the hands and of the left foot since April, 1900. Her family history was unimportant. She had been a laundress for several years, and had suffered much from indigestion, but had never suffered from any acute disease. Alcoholism was denied.

For a month before the onset of the weakness she had suffered from a moderately severe attack of rheumatism in both feet—pain and swelling at the ankle-joints being the most marked signs. One morning, as the rheumatism was subsiding, she woke up to find her right ankle and left hand weak, and the weakness continued to increase for a few days, until it was as severe as when she was admitted.

On admission she was a well-built woman of good intelligence, and presenting no signs of alcoholism. The cranial nerves, viscera, and sphincters were all normal.

Motor system.—The trunk muscles were well developed and of good power. There was great weakness of the movements of the upper extremities, chiefly in the hands and wrists (extensor movement being weaker than flexion); the elbow movements were weak, and the shoulder movements, though stronger, were evidently below their normal strength. The arms were affected almost symmetrically, but the right was throughout a little the weaker. In the lower extremities there was great weakness of all movements at the right ankle, where dorsiflexion was almost nil. The left leg was affected, but to a much slighter degree. All the limb muscles were flabby and wasted; the small muscles of both hands were almost completely atrophied, the hand adopting the *main en griffe* position; there was much wasting of the extensor group of the forearms and of the anterior tibial group of the right leg. There were no contractures.

Of sensory changes, numbness of the hands and fingers and tenderness of the calves and legs were well marked; there was also slight but definite anæsthesia to light touches and to pin-pricks on both hands. There was well-marked sweating and congestion of the hands and feet.

Electrically, no faradic response could be obtained in the severely atrophied muscles, which required a strong galvanic current to produce a contraction; there was no polar change.

The knee-jerks were present, the left being brisk and the right considerably diminished. There was no ankle clonus, and the plantar reflexes were absent.

She was treated by massage and galvanism to the limbs, and strychnine hypodermically.

During her six months' stay in hospital she improved greatly in every respect, the hand atrophy and some weakness of flexion of the right ankle alone remaining on her discharge.

Case 3.—Elizabeth A., aged 54, was admitted to the National Hospital on September 8, 1902, complaining of weakness of hands and legs for thirteen months. She is unmarried and her family history is good. In childhood she suffered from scarlet fever and whooping cough, and at the age of 29 she had an attack of "jaundice." Shortly afterwards she went to South Africa, and remained there till a few weeks ago. In July, 1901, she was taken ill with mumps, which ran a fairly usual course; before she was fully convalescent jaundice with headache and vomiting came on, and it was as the jaundice was clearing up that she first noticed weakness of the legs with pain and tenderness of the feet, calves and knees. This got steadily worse, so that in about a month (September) she was unable to stand, and again took to her bed. The condition now began to improve, but a relapse occurred early in November, in which the hands as well as the legs got steadily weaker. She was at her worst about Christmas, 1901, and then had great weakness of the hands with much atrophy of their muscles, considerable weakness of the forearms and some of the upper arm groups; foot movements, especially flexion of the ankle, were much weakened, and all other leg muscles were affected, whilst the trunk muscles became so weak that she was unable to sit up in bed without support. There were no ocular, bulbar, or sphincter troubles.

From that time she slowly began to recover, the trunk muscles first, and then the proximal limb muscles; but the hands and feet have recovered very slightly if at all.

She is a life-long total abstainer, has never had ague, and has

PLATE I.

CASE 3.—Very severe atrophy of all the small muscles of the hands on both sides; tendency to the "claw-hand."

never been exposed to lead poisoning. There was no beri-beri in the district.

On admission she was a thin, pale, well-educated woman of 34; her memory was good, and she was not at all emotional. An enlarged movable kidney on the left side was the only visceral abnormality found. The cranial nerves were normal, and there was no optic atrophy or neuritis.

Her muscles as a rule were poorly developed, and could be easily examined owing to the small amount of subcutaneous fat present. The trunk and proximal limb muscles were of normal power and size, but the forearms and legs showed great muscle wasting and weakness, especially marked in the extensors of the wrists and the flexors of the ankles. The wasting here, however, was quite over-shadowed by that of the hands and feet, where hardly any muscle tissue seemed to remain. The hands adopted a *main en griffe* position, but were quite easily passively moved; the only muscle that could be felt to contract in either hand was the abductor transversus pollicis.

The feet were "dropped" but flaccid, not contractured; they could just be flexed against gravity; all the intrinsic foot muscles seemed to have disappeared; no faradic excitability could be obtained in the feet or hand muscles.

There was a sense of numbness of the hands and fingers and of the feet and toes, but no objective sensory change could be demonstrated here. The skin of the hands and feet was smooth, glossy and perspired freely, but the nails were normal. She could only walk with assistance—a typical "dropped foot" gait.

Up to the present (September 28) no material change has occurred in the condition.[1]

Case 4.—Ellen H., a domestic servant, aged 36, was admitted to the National Hospital on April 1, 1902. She complained of weakness of hands and legs of eight months' duration. The family history was good, and her own health had been good except for an attack of rheumatic fever at the age of 14.

In September, 1901, she had an attack of diphtheria; the attack was of moderate severity, and the local signs soon passed off. About three weeks after the onset of the diphtheria, she noticed her speech was becoming nasal, although she never had regurgitation of fluids through her nose; at the same time double vision and considerable difficulty in reading came on, quickly followed by a sense of heaviness of the hands and feet, the right hand and the left foot being chiefly affected.

[1] See Appendix.

There was at no time any sphincter trouble. As far as can be ascertained, the weakness of the hands and legs progressed for about eight weeks; certainly no improvement began to occur until March, 1902, or about four months after the onset of the paralysis. Thenceforth a slow but steady improvement occurred, the left hand and the right leg especially improving.

With the paralysis had come on pain and great tenderness of the legs, and to a less extent of the forearms; whilst numbness and difficulty in distinguishing objects touched by her hands had also been very marked, but were considerably improved.

Atrophy of muscles began to come on shortly after the onset of the paralysis, and became progressively worse until Christmas, 1901. By this time the small muscles of the right hand were extremely atrophic, those of the left being less so, but still markedly smaller than normal. The forearm and legs were also much wasted, and some general emaciation had also occurred.

The atrophy remained unchanged till March, 1902, since which a steady filling out of the muscles had occurred, only the right hand muscles now being severely wasted.

On admission, she was a fairly well-built woman of healthy appearance; no abnormality was detected in the thoracic or abdominal viscera. The muscles generally were of good size and power, but there was considerable wasting of the forearm and legs (below the knees especially), and the small muscles of the right hand were extremely atrophic; the left hand muscles were also atrophic, but to a much less extent than those of the right hand. In the latter the interossei, abductor pollicis, flexor brevis pollicis and opponens had almost disappeared, and no faradic or galvanic irritability could be found in them. In each forearm the extensors were weaker than the flexors, but both sets of muscles reacted to faradism; it was also noticeable that the wasting was greater on the ulnar than on the radial side of the forearm, and that in firmly grasping an object with her right hand, the hand was not only slightly flexed on the forearm, but was also deflected to the radial side (see photograph, Plate I.). In the left forearm and hand similar changes were also visible, but were much slighter. By September 25, 1902, when the photograph was taken, the left forearm and hand were practically normal, and contrasted markedly with the still atrophic, though also improved, right forearm and hand.

In the lower extremities "foot-drop" was well marked, especially on the left side, and there was corresponding wasting and diminution of faradic excitability of the extensor groups of the

PLATE II.

CASE 4.—The upper figure shows the marked atrophy of the right hand muscles as compared with the left. The lower figure shows the position of the hand in grasping, *i.e.*, slight flexion at wrist with deflection to the radial side.

legs; the small muscles of the feet were very atrophic, especially on the left side; there was very slight contraction of the calf muscles.

Movements at the elbows and knees were all of moderate power, whilst those of the shoulders and hips, as well as all trunk movements, were of normal strength. The ocular, facial, palatal, mandibular and lingual muscles all appeared to act perfectly.

Anæsthesia to all forms of sensation existed markedly on the right hand and wrist and upon the left foot and outer side of the leg below the knee. None could be made out on the left hand and right foot, although in these members also the patient had a subjective sense of numbness. Of the reflexes the supinator jerk was diminished on the right side, but normal on the left; both knee-jerks were rather brisk, but no ankle-jerk could be obtained on either side; the right plantar reflex was of the flexor type, but the left was absent. All the other reflexes were normal. Both hands and both feet were nearly always blue and cold, and sweated profusely.

Under treatment by massage and galvanism, slow but steady improvement has occurred, so that now (September 28) the left upper extremity is almost normal, and much improvement has taken place in the right arm and hand; foot-drop is still present to a slight extent on the left side, but is far less marked. The objective anæsthesia has almost entirely disappeared.

Case 5.—Mary H., a single woman, aged 39, was admitted to the National Hospital in September, 1899, complaining of general weakness and loss of power. There was a strong neurotic history on her father's side, one uncle having suffered from alcoholic insanity and two others from neurasthenia; her mother was suffering from Bright's disease. The patient had always been of a "nervous temperament," and had had much domestic worry of recent years. For a considerable time before admission she had been a housekeeper, and had taken two bottles of stout a day; recently she had had frequent toothache, for the relief of which she took whisky, sometimes as much as eight glasses a day.

About Christmas, 1898, she took a long drive and caught a chill; she found that on her return home her hands were weak and her legs were less steady than usual. Since then the weakness had steadily increased, and slight numbness had come on in the extremities. Cramp pains in arms and legs had been frequent, but no other pain was complained about.

The limbs wasted considerably, especially the upper extremities, so that by September, 1899, although she could still walk, she was unable to button her clothes, &c.

There was a history of some mental enfeeblement and occasional hallucinations during the two months prior to entering the hospital.

On admission she was a moderately wasted woman of good colour. Vision was good and the optic discs were normal. The pupils reacted well to light and on convergence the other cranial nerves were also normal. The muscles as a rule were of poor size, more especially those of the limbs. Trunk movements were of good power and those at the shoulders, elbows, hips and knees were also fairly good. The forearms were considerably weakened and wasted, the extensors of the wrist and fingers having suffered more than the corresponding flexor muscles, although the latter were obviously weak. The small muscles of the hands were greatly weakened and wasted, and were by far the most atrophic muscles found; the lumbricales and interossei had been affected as much as the thenar and hypothenar groups; some fibrillary twitching was to be seen in the thenar muscles. The affection of the legs was comparatively slight, the flexors of the ankle not being markedly more weakened than the extensors. The gait was feeble and shuffling, but not of the "steppage" type. There were no rigid contractures.

Of sensory changes, numbness in the hands and feet were present to a slight degree only, but no definite loss of sensibility to light touches or pin-pricks could be found.

The muscles of the legs and arms were slightly tender if squeezed. There was no sphincter defect. The tendon jerks were present in about the normal degree in the upper and lower extremities and were equal on the two sides. The jaw-jerk was present, and the plantar reflexes were of the flexor type.

The only electrical changes found were in the small muscles of the hand, where a well marked reaction of degeneration was present.

The patient was treated in hospital for about six weeks by massage and galvanism, but no material change in the condition had occurred on her discharge.

Case 6.—Henry N., a sea captain, aged 50, was admitted to the National Hospital on November 1, 1897, complaining of weakness of the hands and legs.

His previous history was good, except that he had been constantly exposed to cold and wet (once having been shipwrecked)

and had suffered from erysipelas of the scalp eleven years previous to admission. He was a total abstainer from alcohol, and had never had malaria or any other fever.

About March 1897, he had an acute febrile attack with a temperature of 103°, for which he was admitted to hospital. He was at first supposed to be suffering from enteric fever, but in three or four days the temperature fell to normal and remained so. He was kept in bed for five weeks, and during this time the left leg became gradually weak, quickly followed by a progressive weakening of the hands and right leg; some general wasting also occurred, but there was at no time any difficulty with swallowing or with speaking; the sphincters were unaffected. There was no loss of feeling anywhere.

On admission six months after the onset, he was a powerfully-built man, of good memory. There was no defect of any of the cranial nerves.

There was a great wasting of the interossei, thenar and hypothenar eminences of both hands, more marked in the right than the left; there was also considerable wasting and corresponding weakness of the muscles on the ulnar side of the forearms. The long extensors and flexors of the fingers were weak, but all other muscles in the upper extremities were of good size and power. In the lower extremities there was some atrophy of all the muscles below the knees, and considerable weakness of the calf and anterior muscle groups. The gait was feeble and of the "dropped-foot" type.

The electrical reaction showed nowhere a full reaction of degeneration, but in the weakened muscles there was a diminished excitability to faradism. The supinator-jerks and knee-jerks were equal on both sides and normally brisk; but no plantar reflex or ankle-jerk was noted. No objective sensory changes could be made out.

The patient remained in hospital for three months, during which time no further progress of the disease occurred. He was discharged on February 1, 1898, in a slightly improved condition.

Case 7.—George G., an engineer, aged 22, was admitted to the National Hospital on April 18, 1899, complaining of weakness in the arms and legs of nine months' duration. The family history and previous history were good; he had never taken alcohol, nor had he suffered from ague or tropical fever.

The onset was rather acute whilst he was apparently in good health, and off the Coast of Mauritius. His first symptom was weakness in the right hand, and this was quickly followed by

weakness in the left hand and difficulty in walking. The weakness rapidly increased, and in a few days both upper extremities were weak in all their movements, and he became unable to stand. There was severe pain and tenderness in the legs, especially at night-time, there was never any feeling of numbness, nor any sphincter trouble. He was taken into hospital a few months later and improved whilst there, but on his discharge the weakness again increased until he was admitted to the National Hospital six months after the first sign had occurred.

On admission, he was a well-built young man of fair education. The abdominal and thoracic viscera appeared to be healthy, and no defect was found in the cranial nerves. Motor power was good in the trunk and shoulder muscles, but extension and flexion of the elbows were below normal strength. Flexion of the wrist was weakened, but not so much as extension; all the movements of the hands were very weak, but none were lost. There was marked atrophy of the thenar, hypothenar and interosseous muscles in both hands, and to a less extent there was wasting of the forearm muscles.

In the lower extremities dorsiflexion of the ankle was his weakest movement, and the calf muscles were also considerably weakened; other movements were of good power. There was considerable tenderness of the calves on pressure, and great pain was caused by pressure over the nerve-trunks. There was no objective anæsthesia. The knee-jerks were normal, and the plantar reflexes were present and of the flexor type.

He remained in hospital for three months, being treated by massage and galvanism; he steadily improved, and on his discharge he had almost completely recovered, only a little weakness and atrophy of the hand muscles remaining.

Clinical Condition.

At the stage when they came under observation the cases recorded above all showed a well-marked atrophy of the small muscles of the hands, together with weakness of the extensors of the wrist and of the flexors of the ankle. The atrophy of the small muscles of the hand in five of the cases reached a severe degree, and especially in Case 3, where only the slightest contractions were possible in the interossei, lumbricales, thenar, or hypothenar muscles. In the more severe cases there was no reaction to the faradic

current in the hand muscles, and diminished reaction in the extensor group of the forearms and in the flexor group of the ankle. In other words, there was an atrophic paralysis of the peripheral type, a paralysis in which the most distal muscles had suffered severely, and in which the proximal muscles were only slightly or not at all affected. In none of the cases did the muscles particularly affected correspond to particular peripheral nerves; the distribution of atrophy corresponded rather to the segments of the cord, the first dorsal supply being especially picked out.

A marked feature of these cases was the absence of rigid contractures. The reason for this appeared to be twofold: firstly, because there was little or no pain on active or passive movement, so that the limbs were kept constantly supple; and secondly, because with the severe atrophy and loss of power of particular muscles there always occurred weakening of the neighbouring muscles.

In all the cases sensory changes, though present, were comparatively slight. They were most marked in Case 4, in which patient definite objective anæsthesias could be made out. All but one of the patients complained of *numbness* in the extremities at some period of the disease, but, as a rule, this sensation was only temporary, and was not noted after admission to hospital. The most prominent sensory sign in all the cases was *muscle tenderness* and tenderness on pressure over the nerve-trunks in the limbs; this persisted in every case until admission, although in Case 1 the most severe grade of the disease had occurred some three years previously. The sensory changes found were thus similar in all respects to those seen in ordinary alcoholic neuritis, but were much less severe at all periods of the disease. In none of the cases was any change found in the fundus oculi.

Case 1 was the only case in which sphincter trouble had occurred; bulbar signs also only occurred in this case at its worst stage and in the case which followed diphtheria, so that, apart from the well-known selective action of the diphtheria toxine in paralysing the palate and ocular muscles, it might be said that cases of the kind recorded here do not show signs of involvement of the cranial nerves, except in

those instances in which a severe and widespread paralysis exists.

Diagnosis.

None of the cases were seen during the progress of the acute symptoms in the early stages. Had they been seen then, there is little doubt that the diagnosis would have been very difficult and that they would have been called multiple neuritis, Landry's acute ascending paralysis, or possibly polio-myelitis. The rapidity of onset of the nervous symptoms was extremely variable, varying from a few days (as in Case 7), to nearly seven months (as in Case 1). With regard to the acute cases, the resemblance to Landry's paralysis, must have been extremely striking—the rapid spread of paralysis from the periphery to the central muscle groups, the slight sensory signs, the slight involvement of the sphincters and the absence of tendency to the formation of bed-sores. In none of the cases recorded was I able to get any account of the electrical excitability of the muscles in the early stages. From the histories given, atrophy of muscle appeared only to come on late in the disease and would not, therefore, assist in the diagnosis at an early stage.

The diagnosis from pure acute or sub-acute polio-myelitis would have been less difficult in the early stages, owing to the sensory signs present. All the cases gave a history of muscle tenderness, and in most of them numbness of the extremities, a sensation of tingling or (spontaneous) pain in the limbs were present, and from the patients' accounts were much more severe and persistent than is usually seen in acute anterior polio-myelitis. The distribution of the paralysis would also have given a clue to the character of the disease in most cases, for although the signs were as a rule mainly motor, there was a well-marked symmetry of affection both in the upper and lower extremities, which would strongly suggest rather a general toxic or inflammatory condition than a focal polio-myelitis. The fact of the disease occurring in adults would not of course of itself negative a diagnosis of acute polio-myelitis.

Later in the disease, particularly at the stage when the

cases were seen in hospital, the diagnosis was in several cases a matter of considerable difficulty at first. It looked as though we had to deal with a patient who had suffered from some acute paralytic condition upon which had been grafted as it were a chronic progressive muscular atrophy. Certainly the resemblance to the Aran-Duchenne type of the latter disease was very striking—the claw hand with atrophy of hand muscles which showed the electrical changes of degeneration, with more or less definite atrophy of other muscles, almost exactly resembled what is seen in progressive muscular atrophy; but the diagnosis of this disease in association with an old neuritic condition was clearly negatived by the course of the affection and the regularity with which one or both of the knee-jerks was found impaired or lost. It is almost unknown in the Aran-Duchenne form of progressive muscular atrophy, to meet with a patient whose knee-jerks are not brisk, except in association with definite atrophy of the quadriceps muscle. In none of the recorded cases was there such a definite atrophy, and in none was there any exaltation of the tendon jerks in the lower limbs; ankle clonus was never found, and the plantar reflex was usually deficient or absent, and when present was always of the flexor type. In only one case also was there any contracture of the calf muscle, and even here (as in the other cases), the lower limbs were quite flaccid. The course of the disease was even more certain evidence that the condition was not one of progressive muscular atrophy. Despite the great wasting of muscles that had occurred in some of the cases, all the patients under observation tended gradually but constantly to improve. Even the hand muscles have filled out again after appearing almost absent, as has been especially noticed in Case 4 during the six months she has been under observation.

The diagnosis of multiple neuritis could not be excluded in any of the cases. In each of them there was the same type of atrophy and weakness with muscle-tenderness, largely symmetrical in distribution and with diminished tendon-jerks. The most marked differences from the usual

form of polyneuritis were—(1) the great atrophy of the intrinsic muscles of the hands; (2) the comparative slightness of sensory changes; (3) the absence as a rule of contractures and (4) the integrity of the psychical condition.

Prognosis.

In all the cases at the stage at which they first came under observation, the prognosis was good in that they tended constantly to lose their sensory signs and to gain power in the affected muscle groups. The hand muscles appeared to be the last to recover, and as far as it has been yet possible to trace the cases, it would seem that years may elapse without full recovery occurring. Nevertheless in all the cases a steady if slow improvement was the rule. In only two of the seven cases was there a history of anything approaching a relapse; all improved under hospital treatment.

Etiology.

Five of the cases gave a history of some febrile condition preceding the onset of the disease, viz., rheumatism (in two cases), diphtheria, mumps, and some pyrexial disease of unknown origin in one case each. In one a definite history of alcoholism was found; in the last case no etiological factor could be made out. As compared with the peripheral neuritis usually seen, it is remarkable that only one of the seven cases might be of alcoholic origin; it is also worthy of note that all of the above factors have also been recorded as antecedents of Landry's paralysis. The severity of the antecedent disease does not seem to have been at all commensurate with the degree of weakness following; for example, in Case 1 the attack of rheumatism was extremely slight, whilst the paralysis ultimately became very severe.

Pathology.

In none of the cases did a fatal termination ensue,[1] so that the morbid anatomy and pathology can only be inferred from clinical considerations, and from a comparison with

[1] See Appendix.

what has been found in similar but fatal cases. Regarded from a purely clinical standpoint it is difficult not to conclude that we are here dealing with a disease which has affected not only the peripheral nerves but the spinal cord. Referring to progressive muscular atrophy, Gowers (1) states that "cases are met with (although not frequently) that present every gradation to subacute polio-myelitis in one direction, and perhaps also to polyneuritis in another." Clinically, the cases reported here appear to be of this intermediate form. If the severe atrophy of the hand muscles (as shown in the photographs) is to be considered as solely a pheripheral nerve lesion, then it must be that particular parts only of peripheral nerves are involved, for the atrophy is as severe in those hand muscles supplied by the median as in those supplied by the ulnar nerve, whilst many muscles of the forearm supplied by the median have remained of fair power. It seems much more rational to suppose that we have here to deal with a toxic affection of the lower neurones, the motor neurones being much more severely affected than the sensory.

On this hypothesis it would be comparatively easy to understand why a mixed motor and sensory nerve like the median should have lost some of its functions whilst others remain. For we should then be dealing with a kind of system degeneration, in which the fibres supplying the muscles subserving the more highly organised movements in the upper extremities are the ones which suffer first and most. We are, however, bound to assume also that the toxine, or more probably toxines, do not act solely on the lower motor neurones, but also upon the lower sensory neurones, although to a much slighter degree; otherwise it is impossible to explain the symptoms of persistent muscle-tenderness, numbness, and anæsthesia which have been noted. This view of the pathology of these cases accords well with the findings of Batten (2) in cases of diphtheritic paralysis; he found "that the dominant lesion in diphtheritic paralysis is a parenchymatous degeneration of the myelin sheath of the nerves. . . . It seems almost certain that a general poison like that of diphtheria must

act on the whole neurone, and . . . that the effect of the poison manifests itself at least in fatal cases in the myelin sheath, and not in the cell-body." However true it may be that in ordinary forms of diphtheritic paralysis there is no change in the cell-bodies, yet it is difficult to believe that cases like those recorded here with long persistent local atrophies are due purely to peripheral nerve affections.

A case very similar to these was published this year by Luzzetto (3), in which malaria appeared to be the cause of the paralysis. The patient rapidly developed paralysis of the hand muscles and of the extensor groups of the forearms, with muscle-tenderness, but no objective sensory change; marked atrophy of the thenar and hypothenar muscles followed, and the patient died of pneumonia about two months after the onset of the nervous symptoms. Marked degenerative changes were found in the nerves and in the anterior horn-cells, and Luzzetto concluded that the cord changes were not secondary to the nerve changes, but that the whole neurone was involved simultaneously.

Another case in many respects resembling those under discussion has been published by Stewart (4). The patient was a woman of 33 years of age, and seven months pregnant at the time of the onset of the disease. No febrile attack preceded the illness, and no other toxic cause could be discovered. The symptoms were numbness of the hands and feet, much tenderness of the calves, and some anæsthesia with atrophy of muscles in the upper and lower extremities. The disease progressed for about six months, the patient dying of pneumonia. The nerves here showed both parenchymatous and interstitial changes, evidently a true neuritis. There was also a doubtful inflammatory condition in the capsule around the anterior horn-cells of the cord, and undoubted chromolytic changes, and in places atrophy of many of the cells.

The cases recorded here appear to correspond clinically rather to the first than to the second of these cases, in that, in Stewart's case, sensory changes were very marked, almost if not quite as marked as in cases of alcoholic neuritis. Possibly the reason for this difference in the clinical symp-

toms is that the first recorded (malarial) case, was one of toxic degeneration and not of true neuritis; whereas in the second case there was a marked inflammatory condition of the peripheral nerves. I think the distinction is an important one, although it is quite likely that the two conditions may be present in a single case. It would appear probable that when the nervous system is suddenly flooded by toxines the full effects of the poison may be developed, and a true neuritis ensue; whereas if the same toxine were only administered in small doses over a longer period, a selective action might ensue, and cause a degenerative as opposed to an inflammatory reaction. It must also be true that certain of the toxines causing flaccid palsies tend rather to produce inflammatory than degenerative results and *vice versâ*; for instance, diphtheria only rarely causes any interstitial inflammation of peripheral nerves, whereas it is almost the rule in the alcoholic palsies to get an interstitial neuritis developed. Toxines like those of influenza, rheumatism, mumps, &c., would appear to approach more closely to the diphtheritic type, *i.e.*, to cause parenchymatous degeneration rather than interstitial neuritis, and it is not surprising to find the symptoms of the "neuritis" following these diseases differing in a more or less marked degree from those seen in the more common (alcoholic) form of multiple neuritis.

At the present time it is impossible to discuss the pathological relationship between these cases and Landry's paralysis. The latter disease is a clinical symptom-complex, and its pathology is as yet uncertain. Raymond (5) considers that polyneuritis, poliomyelitis and Landry's paralysis are diseases that cannot be sharply distinguished from one another, and that they have the same etiology. Redlich, too, believes that polio-myelitis and polyneuritis are the same affection with different localisations. On the other hand, E. W. Taylor (6) denies that there is any certain evidence of a coincident inflammation of the ventral horn and the peripheral nerves.

I am inclined to think the balance of evidence is in favour of a coincident affection of the whole of the lower neurones, possibly more marked in one part of them than

another; that in these cases the motor neurone is more severely diseased than the sensory neurone; that in the cases recorded here, there is a parenchymatous degeneration rather than a true inflammation; and lastly, that although at some stages of the disease there is a lesion sufficiently severe to destroy for the time being the functions of the main mass of the nerve-fibres to the limbs, that in great part the lesion falls short of absolute destruction, so that a large amount of repair is possible in all cases, and that in some cases the repair of tissue and consequent recovery of function may be complete.

Conclusions.

(1) There is a clinical type which is usually the sequel of acute specific fevers, which resembles the paralysis seen in multiple neuritis, but which is associated with great atrophy of the hand muscles. It usually begins about the second or third week after the febrile condition, and involves the muscles from the periphery to the trunk to a varying extent. It may progress for a few days only, or for several months. Sensory signs are present, but slight in degree. Although the condition somewhat resembles progressive muscular atrophy, the prognosis and etiology of the two conditions are probably widely different from one another.

(2) After a certain stage, when once definite improvement has begun, relapses are not common, and there is a constant tendency to improvement. Even years after the subsidence of the acute condition considerable improvement may still take place, the small muscles of the hands being the last to recover. Contractures are rarely developed.

(3) Probably the condition is one of toxic degeneration of the lower neurones, the motor neurones being more particularly affected.

Appendix.

A further report of Case 3, with results of *post-mortem* examination.

On November 17, 1902, whilst still in hospital, the patient began to complain of obscure pain in the back and a general

sense of uneasiness. Nocturnal restlessness and insomnia came on, and the enlarged kidney became slightly more tender on pressure; there was a light cloud of albumen in the urine. This condition persisted for several days, and on November 24 she complained of feeling much weaker, and was unable to sit up in bed. It was then found that all the tendon-jerks had disappeared since the previous week. Numbness and tingling came on in the hands and feet, and next day there was incontinence of fæces and urine (although she was fully conscious) and respiration was embarrassed. No bulbar signs developed, but she died in the afternoon of November 25, of respiratory failure. The mode of death was almost identical with that which occurred in a case of Landry's paralysis which was in hospital shortly afterwards.

At the autopsy held next day, there was found congenital cystic disease of both kidneys of considerable severity; both kidneys were very much enlarged, but contained so much normal parenchyma that it is almost certain that this was not the direct cause of death. The other abdominal and thoracic viscera were normal. The spinal cord was smaller than usual, and most of the nerve-roots and peripheral nerves originating from the cervical and lumbo-sacral enlargement were thin and wasted.

Attempts to cultivate bacteria from the cerebro-spinal fluid and spinal cord, gave negative results (gelatin, agar-agar and bouillon). The central nervous system was removed and hardened partly in formalin and partly in absolute alcohol, and sections were prepared by the methods of Marchi, Weigert, Nissl and van Giesson; a few sections were also stained by hæmatoxylin and eosin. The peripheral nerves and posterior root ganglia were similarly treated, and parts of apparently normal and diseased muscles were stained by hæmatoxylin and eosin.

The following microscopic changes were found:—

Muscles.—The erector spinæ, infra-spinatus and flexor muscles of the forearm were normal. The pronator quadratus was moderately affected, as were the extensors of the wrist. The lumbricales, flexor brevis pollicis, abductor pollicis, opponens pollicis and hypothenar muscles all showed very marked changes from the normal.

In the diseased muscles there was found great thickening of the arteries and a proportional increase in the general fibrous tissue; in all probability there was no actual increase in the amount of fibrous tissue, the apparent increase being due to wasting of the muscle-tissue. There was no small-celled infiltration. The tendon appeared normal, and the muscle spindles

remaining completely unaffected side by side with atrophic muscle-fibres, were very prominent and proportionately numerous ; in every case the muscle-fibres contained in the muscle-spindles remained normal.

Atrophy of muscle-fibres has occurred very diffusely ; in some muscle-groups, it is true, nearly every fibre is atrophic, but the rule is for the degenerated fibres to lie side by side with normal ones. In those muscles which are only partly affected, only certain of the muscle prisms show any atrophic fibres ; in a severely affected muscle (the lumbricales for instance) every prism contains some degenerated fibres. The affected fibres are much reduced in size—to about one-sixth of their normal cross section ; they stain more darkly than usual but preserve their striation perfectly. They are not particularly granular, and contain no fat ; they have not lost their regularity of outline.

Nerves.—The ulnar nerves were the most severely affected of the nerves examined. Hæmatoxylin stained sections showed marked thickening of the coats of the arteries, but no increase in the number of nuclei present nor any proliferation of interstitial tissue. By the Weigert method marked changes were found. Whole strands of fibres were degenerated and showed simply beads of unabsorbed myelin instead of a continuous medullary sheath. Many very finely medullated fibres were seen which showed fusiform swellings of myelin—probably regenerating fibres. About one-eighth of the fibres were of the normal size ; about one-third of the fibres were reduced to about half the normal diameter ; whilst the rest consisted of the very fine fibres with fusiform swellings. As in the case of the muscles, the fibres affected were scattered very diffusely throughout the nerve, and did not lie in special bundles. By the Marchi method no degenerative changes could be made out ; in all probability the fragmentation of myelin seen in some of the fibres by the Weigert method was an artefact.

Posterior root ganglia.—These all appeared to be normal in every respect.

Medulla and spinal cord.—All the sections of the medulla were normal ; no sign of any affection of the hypoglossal or vagus nuclei could be found.

In the spinal cord no abnormality could be detected by the Marchi or Weigert-Pal methods in any of the tracts. Sections stained by the van Giesson method showed an extremely marked change in the vessels of the whole spinal cord ; these changes were most marked in the cervical enlargement, but were also

present to a less extent in the lumbar enlargement and dorsal region. A section taken at the level of the eighth cervical segment (where the affection was severe) showed a great thickening of the walls of all the arteries, which appeared to be embedded in a faintly striated material with a peculiarly vitreous appearance; it stained faintly with basic dyes, and bright red with van Giesson's solution, but did not give the amyloid reaction. The septa seemed to be entirely composed of this material, and were greatly swollen; the pia mater immediately around the cord was similarly though less severely affected. Where vessels were cut in cross-section, this material was faintly laminated as it lay around them; a few nuclei were scattered irregularly through it, but otherwise it presented an almost homogeneous appearance. The vessels and supporting tissue of the nerve-roots at their points of exit from the cord were similarly affected. Throughout the endothelial coat of the blood-vessels was unaffected and none of the vessels appeared to be thrombosed.

The *cell changes* were almost entirely confined to the anterior horns, and were extremely marked in both the cervical and lumbar enlargements. A section taken at the level of the fourth cervical segment showed about a sixth of the anterior horn cells to be normal; a few cells were shrunken and deeply-staining, but there was no evidence of any cell having completely disappeared. The rest of the cells were in various stages of tigrolysis; they were swollen, stained homogeneously a faint blue colour (Nissl method), no tigroid bodies being visible; in most of the cells the nucleus was eccentric.

At the level of the seventh cervical segment the antero-lateral group was the one most markedly affected, only a few dark-staining, shrunken remnants remaining; in the other groups of cells a little acute change was present, but in the main they were normal. At the level of the first dorsal segment much atrophy of cells was apparent. In one section not a single cell was left in the entire anterior horn, and in most only a few ragged, broken remnants could be found to represent the horn-cells. In the second dorsal segment most of the anterior horn-cells were atrophic, but a few which had survived showed tigrolysis.

In the lumbar region there was no evidence of any cells having disappeared, and none were seen in an atrophic condition. Nearly every cell was much swollen, with excentration of the nucleus and marked tigrolysis; a few cells—not more than a tenth of the entire number—were apparently normal.

It was thus clear that as a whole two kinds of cell change

were present. In the first place, some of the cells had atrophied as a result of a long-standing process, whilst others were in a state of tigrolysis as a result of the morbid process which was the immediate cause of the patient's death.

The results of pathological investigation thus largely bear out what had previously been surmised. There can be little doubt that this patient succumbed to the third attack of a toxæmia which caused degeneration of the lower neurones. I would again emphasise the remarkable similarity between the terminal attack and the clinical condition seen in Landry's paralysis. If this patient had come into hospital for the first time during the final acute attack, and had shown no signs of previous nervous disease, there can be no doubt that a diagnosis of Landry's paralysis would have been made without hesitation. Whatever the pathological relationship between the two sets of conditions may be, it would seem that clinically one would have been justified in regarding this case as one of relapsing Landry's paralysis. The condition of the kidneys in this case may have been a factor predisposing to the disease by deficient elimination of toxins; but seeing that the amount of urine passed was never below the normal, I do not think they played any essential part in the production of the disease.

I am deeply indebted to Dr. Farquhar Buzzard for his care in the preparation of the specimens, and to Dr. J. S. Collier for his assistance in describing the pathological changes.

Bibliography.

(1) Gowers. "Diseases of the Nervous System," 3rd edition, vol. i., p. 532.
(2) Batten. "Diphtheritic Palsy." *Transactions of the Pathological Society of London*, 1899.
(3) Luzzetto. *Berlin Klinische Woch.*, April, 1902.
(4) Stewart. *Philadelphia Medical Journal*, May, 1901.
(5) Raymond. Oppenheim's "Lehrbuch der Nervenkrankheiten," 2nd edition, p. 394.
(6) Taylor. "Poliomyelitis." *Journal of Mental and Nervous Diseases*, 1901.

ON CERTAIN BLOOD CHANGES IN IDIOPATHIC EPILEPSY.

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THE following research was suggested to the writer by Dr. F. W. Mott, and the work has been carried out in the laboratory of the London County Council, Claybury; the clinical material was obtained from Claybury Asylum. The writer desires to express his deep indebtedness to Dr. Mott for having suggested the investigation, for the use of the Claybury laboratory and for numerous practical hints; to Dr. J. S. Bolton for his assistance and suggestions, and to Dr. Robert Jones for permission to use the clinical material in the Asylum, and for the facilities which he afforded him to obtain it.

In all, forty cases have been investigated, and in twenty of these a differential count of the leucocytes has been made. In all the cases the alkalinity of the blood has been estimated, and in some of the cases the effect of different drugs on the alkalinity has been determined.

The paper commences with a historical account of the previous work which has been done on the subject, and this is followed by a description of the method which has been used during the present research; an account of the cases which have been used and the results which have been obtained are then introduced; and the paper concludes with a short summary of the results of the investigation.

THE ALKALINITY.

Under normal conditions the reaction of human blood is alkaline. The alkalinity is due to the presence of two salts, *e.g.*, bicarbonate of soda $NaHCO_3$ and disodic phosphate

Na_2HPO_4. These two salts are acid salts, and are readily dissociated when brought in contact with an indicator such as litmus, forming a coloured salt. Phenolphthalein when used as an indicator gives a neutral reaction owing to the fact that it does not possess the power of dissociating these acid salts, and for this reason it cannot be employed. Thus the blood is an alkaline fluid in virtue of these two salts, which are bases in combination with very weak acids.

Historical.

Up to the present time various investigations have been carried out, and different methods used to estimate the alkalinity of the blood. The earlier investigators used the titration method. Luntz (1) titrated with phosphoric acid; Lassar (2) titrated with oxalic acid. The same objections apply to both these methods—the amount of blood required is too large, and the solution of these organic acids becomes weaker when exposed to light and air. Leibrich (3) used slabs of plaster of Paris impregnated with litmus—a drop of blood was applied to the slab—the blood corpuscles were retained on the surface. The plasma soaked in and reacted with the absorbed litmus. Schäfer used sheets of glazed paper impregnated with litmus.

These methods were improved upon by Landois (4) in 1884. As this method has been in extensive use it may be briefly described. Blood is mixed with a solution of sulphate of soda and titrated with tartaric acid, the neutral point being estimated with litmus paper. The principle of the method consists in the prevention of coagulation by the saline solution, while the alkalinity is neutralised by the titration with tartaric acid, thus $\frac{7.5}{100}$ solution of tartaric acid is added in graduated amounts to the sulphate of soda solution. Solution 1 will contain $\frac{100 \text{ acid}}{10 \text{ sulphate}}$, solution 2 $\frac{20 \text{ acid}}{90 \text{ sulphate}}$, and so on to solution 10 $\frac{10 \text{ acid}}{100 \text{ sulphate}}$. Equal quantities of blood and one of these solutions are taken up in a pipette, and thoroughly mixed in a watch-glass, and the reaction tested with litmus paper. If the mixture is alkaline, then the next strongest acid solution is taken, and so on until the neutral point is obtained.

Drouin improved this method by titrating with oxalic acid. Again the objection is that too much blood is required, also the presence of the red blood corpuscles necessitates dilution with the saline solution, thus increasing the difficulty of accurately estimating the neutral point. In this method the alkalinity of the blood plasma and corpuscles is estimated, and in order to do this efficiently, titration must be carried out slowly and at the body temperature, so that all the corpuscles are broken down.

Haycraft and Williamson's method (5) consists of a series of glazed litmus paper treated with different strengths of sulphuric acid. This gives a series of papers of graduated acidity. A drop of blood is brought in contact with a paper of a certain strength for ten seconds, then dipped in water, and the reaction noted. The method is a simple one, but the results are not accurate enough.

Wright's method (6), which is used in this investigation and described in full. Wright claims many advantages—the quantity of blood required is small, the red blood corpuscles are completely separated from the serum, the alkalinity can be tested in a few hours, and from a clinical point of view the alkalinity of the serum is the more important because it comes into such close contact with the tissues, and may be taken as an index to the changes taking place in the circulating blood.

Physiology.

The alkalinity undergoes a diurnal variation, being lowest in the morning, gradually rising in the afternoon, and becoming less again in the evening (7). It is increased during digestion, owing to the passage of bicarbonate of soda from the stomach to the blood. It is decreased after severe muscular exertion, probably owing to the entrance of the products of muscular metabolism, *e.g.*, sarcolactic and carbonic acids, into the blood. Apart from these two conditions, the alkalinity is maintained at a constant level, varies within physiological limits, and may be taken as an index of the amount and activity of oxidation within the tissues.

Pathology.

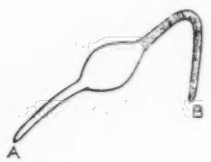
Numerous observations are recorded, noting the changes in the alkalinity in disease. These changes are constant, and manifest themselves in a diminution of the alkalinity, in diseases of the blood, *e.g.*, leucocythæmia and pernicious anæmia; in febrile and cachetic conditions; in diabetes; and especially in diabetic coma, cholera, jaundice, gout, and rheumatism. Also in certain mental diseases, *e.g.*, dementia paralytica, and epilepsy.

Charon and Biche (8), working with Landois' method, found a diminution in epilepsy, and came to the conclusion "that the epileptic attacks present nearly constant variations and in inverse relationship to the variations in the alkalinity of the blood."

Lui (9), a year later, confirmed the diminution in the alkalinity.

Wright's Method.

The thumb is cleansed with soap and water and sterilised with 5 per cent. solution of formalin—a solution of carbolic acid is inadmissible, as it interferes with the alkalinity of the blood. An incision is then made with a lancet, and a copious supply of blood is obtained; it is unnecessary to apply pressure to the thumb. The blood is collected in capillary tubes by means of gravity and capillary attraction, or if necessary by suction at the other end of the tube.



B is then sealed up in the blowpipe flame, the tube inverted, then A is sealed. It may be left suspended for twenty-four hours, during which the clear plasma will

gravitate to the A end, the corpuscles being retained at the B end. The method used by the writer was to suspend the tube for some hours, and then to centrifuge.

Preparation of Acid Solutions and Indicator for the Analyses.

A solution of sulphuric acid is accurately standardised by precipitating with barium chloride and weighing the barium sulphate thus produced. The mother solution used is of the following value: 1 cc. = ·04155 grammes of H_2SO_4 (mean of six analyses). Dilutions of various strengths are made from this acid by running the calculated amount for the strength from the burette into a graduated cylinder and adding the requisite amount of distilled water. The dilutions first used were 10, 20, 30, 40, 60. These were supplemented by other dilutions as these became necessary during the progress of the investigation.

10-fold	dilution	1,000	cc.	=	4·155	grammes of H_2SO_4.
20	,,	,,	,,		2·0755	,, ,,
23	,,	,,	,,		1·806	,, ,,
24	,,	,,	,,		1·731	,, ,,
25	,,	,,	,,		1·662	,, ,,
26	,,	,,	,,		1·59	,, ,,
27	,,	,,	,,		1·538	,, ,,
28	,,	,,	,,		1·48	,, ,,
29	,,	,,	,,		1·43	,, ,,
30	,,	,,	,,		1·385	,, ,,
33	,,	,,	,,		1·26	,, ,,
35	,,	,,	,,		1·18	,, ,,
37	,,	,,	,,		1·12	,, ,,
40	,,	,,	,,		1·0387	,, ,,
50	,,	,,	,,		·831	,, ,,
60	,,	,,	,,		·6925	,, ,,
70	,,	,,	,,		·5935	,, ,,

The indicator used was the No. 6 special litmus paper of Grübler. This was treated according to Wright with an extremely dilute acid solution (1 in 20,000 of hydrochloric acid), washed with distilled water, and dried at 100° C.

Titration of Serum against the Standard Acid Solutions.

A capillary pipette is inserted into the serum, and the latter is allowed to flow into the tube for a distance of 2 cm. The serum is allowed to run up the pipette for a short distance in order to introduce an air bubble, and then a mark is made with a blue pencil. The end of the pipette is now quickly inserted into a solution of acid of a known strength, say the 30-fold dilution, and the acid solution is allowed to run in until the lower end of the serum column runs up to the blue mark. In this way an equal quantity of serum and of an acid of known strength is obtained. The contents of the pipette are blown out on to a clean watch glass and thoroughly mixed with the end of the pipette, aspirated, blown out again, and so on until mixing is complete. Finally the mixture is once more taken into the pipette, and a drop or two are blown on to a piece of the prepared litmus paper. The reaction is noted, and if the neutral point has not been accurately estimated fresh titrations are carried out with acids of greater or less strength until the desired reaction is obtained. Great care must be taken to standardise the acid in the first instance. Wright's results are given as dilutions of the chemically normal H_2SO_4 acid, but the acid employed in this investigation was of different strength, thus :—

1,000 cc. = 4·155 grammes of H_2SO_4
1,000 cc. = 4·9 grammes of H_2SO_4 (Wright's).

The alkalinity has been returned as the amount of H_2SO_4 in 1,000 cc. of the acid solution employed, which would exactly neutralise 1,000 cc. of serum. Thus, by alkalinity 1·385 is meant that 1,000 cc. of a solution containing this amount of H_2SO_4 would exactly neutralise the alkaline properties of 1,000 cc. of the serum.

For obtaining the normal alkalinity control cases have been selected from the staff of Claybury Asylum—physicians, clerks, porters, and attendants. Care was taken to avoid the time during which the alkalinity is said to vary, *e.g.*, after food and after severe muscular exercise. Blood was taken at a stated time, 11 a.m., on successive days from each case.

The average obtained was 1,662; one case, W. H. F., showed the highest, 1,806; this was obtained on three occasions. In all twenty cases were examined. The control cases were not taken from one class in order to show the constancy of the alkalinity, for in spite of the different conditions of living, such as diet, habits, &c., between the cases, the alkalinity was maintained at a constant value, and varied within physiological limits.

In the case of the epileptics, blood was taken from each patient at 11 a.m. on successive days during the interparoxysmal period, *i.e.*, an interval of seven days between seizures. The alkalinity varied; two cases showed a normal alkalinity. The average of the forty cases was below that of the control cases.

Leucocytes.

The blood was obtained from the ear in nearly all the cases, and from the thumb in the remainder. The instrument used for the leucocyte count was the ordinary Thoma-Zeiss apparatus; the diluting fluid was the ordinary normal saline solution coloured with methyl violet. In all the cases 256 squares were counted, the co-efficient of error being 2 per cent. Cover glass preparations were taken at the same time, put in the incubator for an hour, held over osmic acid vapour for five minutes, replaced in the incubator for twenty-four hours, then stained with well-diluted Delafield's hæmatoxylin for five minutes, counterstained with eosin for thirty seconds, washed in methylated spirit, absolute alcohol, cleared in xylol, and mounted. In the differential count from 800 to 1,000 leucocytes were counted; four cover glass preparations were used. The nomenclature adopted in the classification of the leucocytes is taken from Clifford Allbutt's "System of Medicine."

(I.) The finely granular oxyphil polymorphonuclear contains numbers of fine granules—nucleus irregular and multipartite, phagocytic, 75 per cent.

(II.) The coarsely granular oxyphil or eosinophile contains large granules—nucleus, horseshoe, or vermiform, not phagocytic, 2 per cent.

(III.) Small hyaline or lymphocyte—nucleus large, protoplasm hyaline, no granules, 20 per cent.

(IV.) Large hyaline, larger amount of protoplasm than the small, 10 per cent.

The total number of leucocytes per cubic millimetre of blood is extremely variable—variations occur in normal individuals at different times—the normal range lies between 6,000 and 10,000. Any number below 6,000 constitutes a hypo-leucocytosis, and above 10,000 a leucocytosis. Physiological leucocytosis occurs in the new-born, in pregnancy, and during digestion. As all the cases are males and adults, the first two are excluded. In taking the leucocyte count in the interparoxysmal period, due attention was paid to the last point, and the time chosen was half an hour before meals, digestion leucocytosis thus being ruled out.

Historical.

Rutherford Macphail (11) was the first observer to note the changes in the blood in mental diseases. He states that in epilepsy the vitality is lowered and the blood is more deteriorated in male than in female patients. Of 100 cases on admission 37 per cent. recorded a lower percentage of red blood corpuscles and 40 per cent. showed a higher percentage than normal; the leucocytes varied within physiological limits. Kroumbmiller (12) who studied the blood in various psychoses, which included twelve cases of epilepsy, states that at the time of the attack the total quantity of leucocytes increases, and that this increase diminishes with every new attack; the leucocytosis is at its highest an hour after the attack. The increase is due to a relative and absolute increase of lymphocytes with a relative decrease of the older cells. He also states that a few hours after the paroxysm the coarsely granular oxyphil cells are increased.

Case 1.—Aged 16, admitted May 31, 1900; duration of epilepsy five years, bodily condition good.

Family history.—Father and mother alive, intemperate. Paternal aunt insane, patient the only child.

Mental condition.—Very dull and feeble-minded, is unable to

add simple numbers, slow in answering questions. After fits is very impulsive and restless. Often has to be held down.

History of fits.—First fit five years ago, when at school. Fits gradually increased in frequency, grand mal; after an attack remains in a state of mental confusion for some hours (five to fourteen).

Record of fits from admission to December 31, 1901.—Day fits 110; night fits 207.

Alkalinity of blood during the interval 1·48.

September 24, 1901.—Seven fits from 8 p.m. to 9.50 p.m. Blood 10 p.m. alkalinity 1·0387. Blood 10.30 p.m. alkalinity 1·26. Blood 11 p.m. alkalinity 1·385. Blood 12 p.m. alkalinity 1·385. Blood 1 a.m. alkalinity 1·43.

The next morning patient was very confused. Blood 10.30 a.m. alkalinity 1·43.

December 20, 1901.—Five fits from 7 a.m. to 7.45 a.m. Blood 9 a.m. alkalinity 1·18. Blood 11 a.m. alkalinity 1·43. Blood 12 a.m. alkalinity 1·48. Blood 3 p.m. alkalinity 1·48.

December 25, 1901.—Five fits from 10 a.m. to 12 noon. Blood 12.30 p.m. alkalinity ·831. Blood 1.30 p.m. alkalinity 1·12. Blood 2.30 p.m. alkalinity 1·385. Blood 5.30 p.m. alkalinity 1·43.

The patient was very confused, would not answer questions, and was very irritable when spoken to.

This mental confusion lasted for eight days, and during this period blood was taken at a stated time—11 a.m. every morning. December 26, alkalinity 1·48; December 27, alkalinity 1·48; December 28, alkalinity 1·48; December 29, alkalinity 1·538; December 30, alkalinity 1·48; December 31, alkalinity 1·59; January 1, alkalinity 1·59; January 2, alkalinity 1·59.

On January 3 he was bright and cheerful, answered questions readily and expressed a desire to get up. From December 20 to January 3, he was not treated for his epilepsy.

January 5.—Was put on potas. bromid. gr. 20, three times a day. This treatment was continued until January 13. During this treatment he had three day fits, and the alkalinity was maintained at 1·538.

January 12, 1902.—About sixty seconds after his blood had been taken, he had a slight fit. Immediately prior to the fit, alkalinity 1·26; half an hour after, alkalinity 1·18; one hour after, alkalinity 1·385; two hours after, alkalinity 1·43; four hours after, alkalinity 1·538.

January 13, 1902.—Was put on suprarenal extract, one capsule three times a day after meals; on the 15th the dose was increased to six per diem. On the 20th reduced to three a day,

and continued until January 29. Whilst under this treatment he had thirty-three day fits and seventeen night fits, which is a distinct increase; the mental confusion, however, was not so great, and he recovered from the after-effects of the paroxysms much sooner than when under the bromide treatment. During the intervals, there were no distinct changes in the blood; the leucocytes appeared normal, the alkalinity was not affected, the pulse was diminished in frequency by eight beats, and the blood pressure was increased.

January 30.—He was given strontii bromid. gr. 15, sodii bicarb. gr. 15, aq. ad ʒj, ʒj three times a day. This treatment was continued for two months. During this time he had four day fits and seventeen night fits, which is a pronounced decrease, the average number of fits per month being six day fits, ten night fits. The alkalinity was maintained at a fairly constant value, and varied from 1·48 to 1·662.

Leucocytes. — Interparoxysmal period, 9,500. Differential count:—Polymorphonuclear, 65 per cent.; large hyaline, 6 per cent.; small hyaline, 25 per cent.; eosinophile, 3 per cent. Ten minutes after seven fits:—Leucocytes, 10,000. Differential count:—Polymorphonuclear, 68 per cent.; large hyaline, 8 per cent.; small hyaline, 23 per cent.; eosinophile, 4 per cent. Sixty minutes later:—Leucocytes, 21,000. Differential count:—Polymorphonuclear, 60 per cent.; eosinophile, 5 per cent.

Case 2.—Aged 18. Admitted August 7, 1900. Duration of epilepsy, nine years; bodily condition good.

Family history.—Father died of acute Bright's disease aged 36, an alcoholic. Mother alive and well; six children, four boys, two girls; patient is the fifth child; the sixth child is also an epileptic.

Mental condition.—Is rational in manner and talk, slight impairment of memory; is very intractable after fits.

History of fits.—Developed his epilepsy at nine years of age; his mother states that he had a fall on his head when six years of age. Grand mal. Recovery from mental confusion gradual; two minutes before a fit the right lower eyelid twitches.

Record of fits from admission to December 31, 1901.—Day fits, 44; night fits, 81.

Alkalinity in the interparoxysmal period, 1·538. Slight fit 8 a.m. Blood 11 a.m. alkalinity 1·385. Blood 2.30 p.m. alkalinity 1·538.

Two fits 9.30 p.m. Blood 10.30 p.m. alkalinity 1.26. Blood 11.30 p.m. alkalinity 1·385. Blood 1 a.m. alkalinity 1·48.

Blood 7.30 p.m. alkalinity 1·59. Blood 11 a.m. alkalinity 1·43. Blood 12 noon alkalinity 1·48. Blood 3 p.m. alkalinity 1.48.

January 12, 1902.—About sixty seconds after his blood had been taken he had a slight fit.

Immediately prior to the fit, alkalinity 1·26; half an hour after, alkalinity 1·18; one hour after, alkalinity 1·385; two hours after, alkalinity 1·43; four hours after, alkalinity 1·538.

Leucocytes.—The study of the blood ten minutes after the fit shows leucocytes 9,500. An hour after:—There is a distinct leucocytosis 14,000. Differential count:—Polymorphonuclear, 60 per cent.; small hyaline, 25 per cent.; large hyaline, 11 per cent.; eosinophile, 4 per cent.

Case 3.—Aged 18. Admitted August 24, 1900. Duration of epilepsy, fourteen years. Bodily condition fair, stature short, suffers from constipation.

Family history.—Father and mother (Jews) dead, both intemperate; patient the only son; one sister alive and healthy. Maternal uncle insane, committed suicide.

Mental condition.—Is simple and childish in manner and talk, is easily confused, mental reaction slow. Answers questions slowly. Memory for recent events impaired.

History of fits.—Said to be healthy and intelligent up to 1886, when his father died suddenly. Soon after this patient had two epileptic fits. Grand mal. Mental confusion lasts about one and a half hours.

Record of fits from admission to December 31, 1901.—Day fits, 275; night fits, 450.

Alkalinity in the interparoxysmal period, 1·48.

December 2.—Eight fits from 10.30 a.m. to 11 a.m.

Blood 11.15 a.m. alkalinity ·831. Blood 12 noon alkalinity 1·26. Blood 1 p.m. alkalinity 1·385. Blood 3 p.m. alkalinity 1·48.

At 4 p.m. patient was very restless and irritable, and a little confused. At 7.30 he had ten very severe fits, and was given an enema of potas. brom. gr. 30, chloral hydrate. gr. 15.

Blood 7.45 p.m. alkalinity 1·18. Blood 8.30 p.m. alkalinity 1·385. Blood 9.30 p.m. alkalinity 1·26. Blood 11.30 p.m. alkalinity 1·48.

During the month of December the potassium bromide was suspended, and he had 97 day fits and 41 night fits.

December 15.—Fifteen fits 11.50 p.m. to 12.30 a.m.

Blood 12.40 a.m. alkalinity ·831. Blood 1 a.m. alkalinity 1·26. Blood 10.30 a.m. alkalinity 1·538.

December 21.—Fourteen fits 8.30 p.m. to 9 p.m.

Blood 9.15 p.m. alkalinity 1·0387. Blood 10 p.m. alkalinity 1·385. Blood 11 p.m. alkalinity 1·43. Blood 12 midnight alkalinity 1·48.

January 13, 1902.—Was put on suprarenal extract, one capsule three times a day after meals. On the 17th the dose was increased to six per diem; on the 22nd the dose was reduced to three per diem. This treatment was continued until February 1. The effects produced were essentially similar to those produced in Case 1. The fits increased in frequency; the record for the eighteen days reads:—11 day fits, 154 night fits. The marked increase of the nocturnal fits is very striking, and is five-fold greater than the average monthly record. The nearest approach to these figures was in June, 1901, when the patient had 121 night fits.

Blood.—No distinct change in the alkalinity, which varied from 1·48 to 1·538. The leucocytes appeared normal.

Pulse.—Diminished in frequency by nine beats on an average, and the blood pressure was increased. January 14, 11 a.m., 125 mm. January 16, 11 a.m., 130 mm. January 18, 11 a.m., 130 mm. January 21, 11 a.m., 145 mm. January 26, 11 a.m., 145 mm.

The effect upon the mental state was good, and the recovery from the confusion following the fit was rapid.

January 30, 1902.—He was put on strontii bromidi gr. 15, sodii bicarb. gr. 15, aq. ad ℥j, ℥j, three times a day.

February 12.—The mixture was given four times a day for twelve days, and from February 24 to the end of March three times a day. Under this treatment the number of fits was considerably decreased, and during the month of February the patient did not have a fit. The alkalinity was maintained at a constant value, *e.g.*, 1·538 to 1·662.

Leucocytes.—Interparoxysmal period, 9,200. Differential count:—Polymorphonuclear, 68 per cent.; large hyaline, 7 per cent.; small hyaline, 22 per cent.; eosinophile, 3 per cent. Forty minutes after eight fits:—Leucocytes, 19,000. Differential count:—Polymorphonuclear, 60 per cent.; large hyaline, 8 per cent.; small hyaline, 30 per cent.; eosinophile, 2 per cent.

Case 4.—Aged 19, admitted May 15, 1900. Duration of epilepsy, seven years. Bodily condition good.

Family history.—Father and mother alive and well. Insanity and phthisis on mother's side. Patient the only child alive; his brother died of phthisis, aged 18.

Mental condition.—Is rational in manner and talk in the intervals. Memory slightly impaired. Is very fanciful and restless after fits, and develops delusions of persecution.

History of Fits.—Developed epilepsy at 12 years of age; the fits gradually increased in frequency; the month before admission he had over 100 fits. Grand mal, mostly nocturnal; recovery from mental confusion rapid.

Record of fits from admission to December 31, 1901.—Day fits, 693; night fits, 830.

Alkalinity in the interparoxysmal period, 1·43; three hours after his blood had been taken the patient had a strong fit—3 p.m. Blood 3.15 p.m. alkalinity 1·0387. Blood 4 p.m. alkalinity 1·26. Blood 5 p.m. alkalinity 1·43. Blood 8 p.m. alkalinity 1·538.

January 13, 1902.—Was put on suprarenal extract, one capsule three times a day. On the 17th the dose was increased to six a day. This treatment was carried out for eighteen days. The fits increased in frequency, but not to such an extent as in Cases 1 and 3. There were no distinct changes in the blood, the leucocytes were normal, but the alkalinity varied; on two occasions it was 1·43.

Pulse.—Diminished in frequency by six beats, the blood pressure was increased. The effect upon the mental state was very pronounced, the after-effects passing off in a short time.

Leucocytes.—Interparoxysmal period, 10,000. Differential count:—Polymorphonuclear, 70 per cent.; large hyaline, 6 per cent.; small hyaline, 21 per cent.; eosinophile, 3 per cent. Four hours after a fit:—Leucocytes, 12,000 Differential count:—Polymorphonuclear, 62 per cent.; large hyaline, 4 per cent.; small hyaline, 30 per cent.; eosinophile, 5 per cent.

Case 5.—Aged 33, admitted October 18, 1893. Duration of epilepsy unknown. Bodily condition fair.

No family history obtained.

Mental condition.—Is dull, lost, and feeble-minded. After fits is restless, and has hallucinations of sight.

History of fits.—Grand mal. Epigastric aura. Mental confusion lasts about three hours.

Record of fits from admission to December 31, 1901.—Day fits, 305 night fits, 448.

Interparoxysmal alkalinity, 1·662, 1·538. Five fits in quick succession. Blood fifteen minutes after, alkalinity ·831. Blood one hour after, alkalinity 1·26. Blood two hours after, alkalinity 1·385. Blood four hours after, alkalinity 1·48. Blood twelve hours after, alkalinity 1·662. Alkalinity during aura, 1·26.

Leucocytes.—Twelve hours after five fits:—Leucocytes, 11,000. Differential count:—Polymorphonuclear, 70 per cent.; large hyaline, 7 per cent.; small hyaline, 18 per cent.; eosinophile, 5 per cent.

Case 6.—Aged 46, admitted September 10, 1896. Duration of epilepsy three years. Bodily condition fair.

Family History.—Father and mother dead. Paternal uncle insane. Patient the only child.

Mental condition.—Is demented; has very little idea of time or place; after fits is very restless and irritable, and develops religious delusions.

History of fits.—Had his first fit three years ago after a drinking bout. Grand mal. Mental confusion lasts about three hours.

Record of fits from admission to December 31, 1901.—Day fits, 81; night fits, 114.

Interparoxysmal alkalinity, 1·662 to 1·538. Two strong fits. Blood 20 minutes after, alkalinity 1·0387. Blood half an hour after, alkalinity 1·12. Blood one hour after, alkalinity 1·26. Blood two hours after, alkalinity 1·43. Blood five hours after, alkalinity 1·538.

Sixty minutes after:—Leucocytes 18,000. Differential count:—Polymorphonuclear, 58 per cent.; large hyaline, 8 per cent.; small hyaline, 33 per cent.; eosinophile, 2 per cent.

Case 7.—Aged 40, admitted May 25, 1895. Duration of epilepsy, ten years; bodily condition good.

Family history.—Father died of pneumonia, an alcoholic; mother alive and healthy; two brothers alive and well.

Mental condition.—Very rambling and incoherent in talk. Memory much impaired especially for recent events; expresses "electrical" delusions.

History of fits.—Had his first fit when 30 years of age, at which time he was travelling with a circus; no history of drink. Grand mal; mental confusion lasts about three hours.

Record of fits from admission to December 31, 1901.—Day fits, 332; night fits, 328.

Interparoxysmal alkalinity, 1·538. Slight fit 10.40 a.m. Blood 11·5 a.m. alkalinity 1·18. Blood 11·45 a.m. alkalinity 1·26. Slight fit 12.10 p.m. Blood 12.30 p.m. alkalinity 1·0387. Blood 1.30 p.m. alkalinity 1·26. Blood 3.30 p.m. alkalinity 1·43. Blood 5.30 p.m. alkalinity 1·538.

Fifty minutes after the second fit:—Leucocytes 19,000.

Differential count :—Polymorphonuclear, 59 per cent. ; large hyaline, 30 per cent. ; small hyaline, 30 per cent. ; eosinophile, 3 per cent.

Case 8.—Aged 19, admitted August 8, 1900. Duration of epilepsy, three years. Bodily condition good.

Family history.—Father died of heart disease, intemperate. Mother alive and healthy. Maternal uncle died of phthisis. Patient was the only child.

Mental condition.—Is very unstable, restless, and irritable, and is given to introspection ; after fits is pugnacious, intractable and suicidal.

History of fits.—Had his first fit when 16 years old, then had a fit every week for six weeks, and then ceased having them for eight weeks. The fits gradually increased in frequency and severity. Grand mal. Recovers quickly from the mental confusion.

Record of fits from admission to December 31, 1901.—Day fits, 94 ; night fits, 236.

Interparoxysmal alkalinity 1·538.—Fit 11.30 a.m. Blood 11.40 a.m. alkalinity 1·12. Blood 12.30 p.m. alkalinity 1·385. Blood 1.30 p.m. alkalinity 1·48. Blood 3.30 p.m. alkalinity 1·538.

Forty minutes after two fits :—Leucocytes, 17,000. Differential count :—Polymorphonuclear, 60 per cent. ; large hyaline, 29 per cent. ; small hyaline, 10 per cent. ; eosinophile, 1 per cent.

Case 9.—Aged 25, admitted December 28, 1900. Duration of epilepsy, fifteen years. Bodily condition good.

Family history.—Father and mother alive and healthy, both intemperate. Two brothers alive and healthy. Patient the third child. One sister simple-minded.

Mental condition.—After fits is very impulsive, religious and emotional. Slight mental impairment.

History of fits.—Developed his epilepsy at 10 years of age. The fits gradually increased in frequency. Grand mal. Laryngeal aura. Recovery from mental confusion gradual (in about three hours).

Interparoxysmal alkalinity 1·538 ; forty seconds before fit 1·26 ; half an hour after, alkalinity 1·18 ; one hour after, alkalinity 1·385 ; two hours after, alkalinity 1·43 ; six hours after, alkalinity 1·538.

Eighty minutes after one fit :—Leucocytes, 12,400. Differential count :—Polymorphonuclear, 68 per cent. ; large hyaline, 23 per cent. ; small hyaline, 6 per cent. ; eosinophile, 3 per cent.

Case 10.—Aged 31, admitted October 24, 1896. Duration of epilepsy, five years. Bodily condition good.

No family history obtained.

Mental condition.—Is dull, stupid, and feeble-minded. Memory very defective, has no idea of time. After fits is irritable, and develops persecutory delusions.

History of fits.—Grand mal. Mental confusion lasts about three hours.

Record of fits from admission to December 31, 1901.—Day fits, 954; night fits, 527.

Interparoxysmal alkalinity, 1·48. Fit 8 a.m. Blood 11 a.m. alkalinity 1·385. Blood 2.30 p.m. alkalinity 1·538. Strong fit 2.45 p.m. Blood 3.30 p.m. alkalinity 1·12. Blood 4.45 p.m. alkalinity 1·385. Blood 8 p.m. alkalinity 1·538. Two fits 9 p.m. Blood 9.15 p.m. alkalinity ·831. Blood 10 p.m. alkalinity 1·12. Blood 11 p.m. alkalinity 1·26. Blood 1 a.m. alkalinity 1·48.

Fifty minutes after the fit:—Leucocytes, 14,000. Differential count:—Polymorphonuclear, 60 per cent.; eosinophile, 3 per cent.; large hyaline, 8 per cent.; small hyaline, 30 per cent.

Case 11.—Aged 21, admitted February 2, 1900. Duration of epilepsy, eight years. Bodily condition fair; suffers from constipation and indigestion.

Family history.—Father alive and well. Mother died of cancer, aged 44. Epilepsy and phthisis on mother's side.

Mental condition.—Is simple in manner and talk; slight mental impairment. After fits is restless and irritable, and develops persecutory delusions.

History of fits.—Had his first fit when 13 years of age. Grand mal. Epigastric aura five minutes before the fit. Recovery from mental confusion gradual.

Record of fits from admission to December 31, 1901.—Day fits, 156; night fits, 107.

Interparoxysmal alkalinity, 1·48. Alkalinity during aura 1·385. Half an hour after fit, 1·18; one hour after fit, 1·385; two hours after fit, 1·48; four hours after fit, 1·538.

Twelve hours after one fit:—Leucocytes, 9,000. Differential count:—Polymorphonuclear, 70 per cent; large hyaline, 7 per cent.; small hyaline, 20 per cent.; eosinophile, 3 per cent.

Case 12.—Aged 46, admitted August 24, 1893. Duration of epilepsy, twenty years. Bodily condition good.

No family history obtained.

Mental condition.—Is very restless and irritable, and talks

much and foolishly on religious subjects. Is very demented; has no idea of time or place.

History of fits.—Has very frequent petit mal seizures. Mental confusion lasts about an hour.

Record of fits from admission to December 31, 1901.—Day fits, 170; night fits, 27.

Alkalinity in the paroxysmal period, 1·538. Alkalinity twenty seconds before a fit, 1·385. Fit 11 a.m. Blood 11.15 a.m. alkalinity 1·385. Blood 12.15 p.m. alkalinity 1·48. Blood 2 p.m. alkalinity 1·538. Three strong fits 7 p.m. Blood 7.20 p.m. alkalinity ·831. Blood 8 p.m. alkalinity 1·12. Blood 9 p.m. alkalinity 1·26. Blood 11 p.m. alkalinity 1·43. Blood 1 a.m. alkalinity 1·48.

One hour after three fits :—Leucocytes, 23,000. Differential count :—Polymorphonuclear, 58 per cent.; large hyaline, 8 per cent.; small hyaline, 32 per cent.; eosinophile, 3 per cent.

Case 13.—Aged 49, admitted November 22, 1897. Duration of epilepsy, 43 years. Bodily condition fair, suffers from constipation and gastric catarrh.

Family history.—Father died in an epileptic fit. Mother alive, intemperate; maternal aunt insane.

Mental condition.—Is dull, stupid, and very demented. After fits is restless, irritable, and impulsive.

History of fits.—Had his first fit when six years of age. He did not have a second until fifteen years later. This was followed by another four years afterwards, then they became more frequent. Grand mal, no aura. Mental confusion lasts about four hours.

Record of fits from admission to December 31, 1901 :—Day fits, 32; night fits, 117.

Interparoxysmal alkalinity, 1·538 : 1·48. Two fits 8.30 p.m. Blood 9 p.m. alkalinity 1·12. Blood 10 p.m. alkalinity 1·26. Blood 12 midnight alkalinity 1·43. Blood 1 a.m. alkalinity 1·48.

One and a half hours after one fit :—Leucocytes, 20,000. Differential count :—Polymorphonuclear, 58 per cent.; large hyaline, 6 per cent.; small hyaline, 39 per cent.; eosinophile, 2 per cent.

Case 14.—Aged 22. Admitted August 22, 1896. Duration of epilepsy, ten years. Bodily condition fair.

Family history.—Father and mother alive and healthy. One brother alive and well.

Mental condition.—Is dull, slow, and feeble-minded. Memory

for recent events defective. After fits is dazed, destructive, and impulsive.

History of fits.—Developed his epilepsy when twelve years of age. Grand mal. Has a severe frontal headache half an hour before the fit. Mental confusion lasts about four and a half hours.

Record of fits from admission to December 31, 1901 :—Day fits, 445; night fits, 834.

Interparoxysmal alkalinity, 1·538 : 1·48. Four fits from 10 a.m. to 11 a.m. Blood 11.30 a.m. alkalinity 1·12. Blood 1 p.m. alkalinity 1·385. Blood 3 p.m. alkalinity 1·48. Blood 6 p.m. alkalinity 1·59. Alkalinity during aura, 1·385.

Six hours after four fits :—Leucocytes, 11,000. Differential count :—Polymorphonuclear, 61 per cent.; large hyaline, 6 per cent.; small hyaline, 25 per cent.; eosinophile, 8 per cent.

Case 15.—Aged 28. Admitted January 25, 1900. Duration of epilepsy, twenty-two years. Bodily condition good.

Family history.—Father alive, very intemperate. Mother dead, cause unknown. Maternal uncle died of paralysis.

Mental condition.—Is very feeble-minded. Memory defective, has no idea of time. After fits is irritable, and has hallucinations of sight.

History of fits.—Developed his epilepsy when six years old. Grand mal. No warning. Mental confusion lasts about three hours.

Record of fits from admission to December 31, 1901.—Day fits, 105; night fits, 172.

Interparoxysmal alkalinity, 1·538. One severe fit 8.30 p.m. Blood 9 p.m. alkalinity 1·26. Blood 10 p.m. alkalinity 1·385. Blood 11 p.m. alkalinity 1·48. Blood 1 a.m. alkalinity 1·59.

Twenty-four hours after two fits :—Leucocytes, 9,000. Differential count :—Polymorphonuclear, 70 per cent.; large hyaline, 4 per cent.; small hyaline, 23 per cent.; eosinophile, 3 per cent.

Case 16.—Aged 31. Admitted December 8, 1899. Duration of epilepsy not known. Bodily condition fair, suffers from constipation.

Mental condition.—Is simple and childish in manner and talk; mental reaction slow, memory very defective.

History of fits.—Grand mal, no aura; mental confusion lasts about three hours.

Record of fits from admission to December 31, 1901.—Day fits, 16; night fits, 162.

Interparoxysmal alkalinity, 1·538 : 1·48. Three fits, ten minutes' interval between the seizures. Blood half an hour after, alkalinity 1·12. Blood one hour after, alkalinity 1·26. Blood three hours after, alkalinity 1·48. Blood five hours after, alkalinity 1·59. Blood twelve hours after, alkalinity 1·59.

Eight hours after one fit :—Leucocytes, 8,000. Differential count :—Polymorphonuclear, 62 per cent. ; large hyaline, 6 per cent. ; small hyaline, 23 per cent. ; eosinophile, 9 per cent.

Case 17.—Aged 34, admitted August 15, 1893. Duration of epilepsy, seven years. Bodily condition fair.

No family history obtained.

Mental condition.—Is very dull and feeble-minded. Memory much impaired, has no idea of time. After fits is restless and intractable.

History of fits.—Had his first fit seven years ago. Grand mal. No warning. Mental confusion lasts three hours.

Record of fits from admission to December 31, 1901.—Day fits, 490 ; night fits, 998.

Interparoxysmal alkalinity, 1·59 : 1·48. Ten minutes after two fits, alkalinity 1·0387. Thirty minutes after two fits, alkalinity 1·16. Two hours after two fits, alkalinity 1·385. Three hours after two fits, alkalinity 1·48. Six hours after two fits, alkalinity 1·59.

Three days after one fit :—Leucocytes, 12,000. Differential count :—Polymorphonuclear, 56 per cent. ; large hyaline, 7 per cent. ; small hyaline, 32 per cent. ; eosinophile, 5 per cent.

Case 18.—Aged 52, admitted September 30, 1896. Duration of epilepsy not known. Bodily condition fair.

No family history obtained.

Mental condition.—Is dull, stupid, and childish in manner and conversation. Memory much impaired. After fits has hallucinations of smell and becomes abusive.

History of fits.—Grand mal, no aura. Mental confusion lasts about three hours.

Record of fits from admission to December 31, 1901.—Day fits, 443 ; night fits, 313.

Interparoxysmal alkalinity, 1·538. Fit 1 p.m. Blood 2 p.m. alkalinity 1·26. Blood 3 p.m. alkalinity 1·385. Blood 5 p.m. alkalinity 1·48. Blood 7.30 p.m. alkalinity 1·59.

Three hours after two fits :—Leucocytes, 13,000. Differential count :—Polpmorphonuclear, 52 per cent. ; large hyaline, 7 per cent. ; small hyaline, 38 per cent. ; eosinophile, 3 per cent.

Case 19.—Aged 19, admitted March 8, 1900. Duration of epilepsy, two years. Bodily condition good.

No family history obtained.

Mental condition.—Is very feeble-minded and is unable to read or write. Habits very faulty. Has very little idea of time or place.

History of fits.—Has always been dull and stupid. Had his first fit two years ago, and during the following twelve months had several slight seizures. A few months before admission he had numerous strong fits. Grand mal. Recovery from mental confusion gradual.

Record of fits from admission to December 31, 1901.—Day fits, 50; night fits, 55.

Interparoxysmal alkalinity, 1·538. Fit 11 a.m. Blood 12 noon alkalinity 1·385. Blood 1 p.m. alkalinity 1·43. Blood 3 p.m. alkalinity 1·48. Blood 7 p.m. alkalinity 1·59.

Four days after one fit:—Leucocytes, 9,000. Differential count:—polymorphonuclear, 68 per cent.; large hyaline, 8 per cent.; small hyaline, 20 per cent.; eosinophile, 4 per cent.

Case 20.—Aged 22, admitted October 18, 1894. Duration of epilepsy, 4 weeks. Bodily condition good.

No family history obtained.

Mental condition.—Is emotional and intractable; memory defective. After fits is intensely noisy, violent, and impulsive, and develops persecutory delusions.

History of fits.—Had his first fit four weeks prior to admission. Grand mal, epigastric aura. Mental confusion lasts about four hours.

Record of fits from admission to December 31, 1901.—Day fits, 303; night fits, 1,845.

Interparoxysmal alkalinity, 1·538 : 1·48. Taken at 2 a.m., 1·43. Two fits in quick succession. Blood half an hour after, alkalinity 1·0387. Blood one hour after, alkalinity 1·26. Blood two hours after, alkalinity 1·43. Blood four hours after, alkalinity 1·59. Blood twenty-four hours after, alkalinity 1·59.

Four hours after two fits:—Leucocytes, 14,000. Differential count:—Polymorphonuclear, 57 per cent.; large hyaline, 5 per cent.; small hyaline, 34 per cent.; eosinophile, 5 per cent.

Case 21.—Aged 26, admitted August 11, 1899. Duration of epilepsy thirteen years. Bodily condition good.

Family history.—Father and mother alive and healthy; two brothers living, healthy; one brother died abroad, cause unknown. Patient has had syphilis.

Mental condition.—Is simple and childish in manner. Does not appreciate his surroundings, is very demented, has very little idea of time.

History of fits.—Had his first fit thirteen years ago. The fits gradually increased in frequency. After fits was very restless and intractable.

Record of fits from admission to December 31, 1901.—Day fits, 172; night fits, 150.

For the last seven months all his fits have been nocturnal. Alkalinity in the interparoxysmal period 1·48. Nine hours before a fit, 1·43. Fit 9.30 p.m. Blood 9.50 p.m. alkalinity 1.12. Blood 10.50 p.m. alkalinity 1.26. Blood 11.50 p.m. alkalinity 1·385. Blood 10.30 a.m. alkalinity 1·538.

Patient was subjected to the suprarenal treatment for twenty-one days, apparently without any effect. The fits did not increase in frequency, and there was no perceptible rise in the blood pressure.

Case 22.—Aged 21, admitted March 22, 1894. Duration of epilepsy, fourteen years. Bodily condition feeble, poorly nourished. Palate high.

No family history obtained.

Mental condition.—Is very simple-minded, is of low intellect, is unable to add simple numbers, rambles incoherently. After fits is irritable, impulsive, and abusive.

History of fits.—Had his first fit when seven years of age. A short time before admission had an attack of status epilepticus. Grand mal, no aura.

Record of fits from admission to December 31, 1901.—Day fits, 531; night fits, 162.

Interparoxysmal alkalinity 1·538 : 1·48. Two slight fits 9 a.m. Blood 9.30 a.m. alkalinity 1·12. Blood 11 a.m. alkalinity 1·43. Blood 1 p.m. alkalinity 1·43. Blood 5 p.m. alkalinity 1·59.

Case 23.—Aged 32, admitted November 8, 1895. Duration of epilepsy, twenty-nine years. Bodily condition fair, suffers from indigestion.

No family history obtained.

Mental condition.—Is dull and feeble-minded; mental reaction is slow; he is easily excited, and is very unstable. Memory very defective; has very little idea of time or place; after fits is violent and impulsive.

History of fits.—Had his first fit when three years of age, and then had three fits a month up to 14 years of age. He had no fits

from 14 to 25, and since the latter age he has had them frequently. Grand mal. Precordial aura, which he describes as "a pleasant feeling as though his heart were stopping."

Record of fits from admission to December 31, 1901. Day fits, 475; night fits, 73.

Interparoxysmal alkalinity 1·48 : 1·43. Alkalinity during aura 1·26; alkalinity thirty minutes after fit, 1·18; alkalinity one hour after fit, 1·26; alkalinity three hours after fit, 1·43; alkalinity six hours after fit, 1·59.

Case 24.—Aged 43, admitted April 30, 1894. Duration of epilepsy, fifteen years. Bodily condition fair; muscular movements very tremulous.

Family history.—Father, mother, and one sister insane at Brookwood Asylum. Brother committed suicide.

Mental condition.—Is dull, morose, and feeble-minded; after fits is restless and wanders aimlessly round the ward; has hallucinations of sight and hearing.

History of fits.—Had his first fit when twenty-eight years of age. Grand mal, no aura. Mental confusion lasts about five hours.

Record of fits from admission to December 31, 1901.—Day fits, 46; night fits, 83.

Interparoxysmal alkalinity 1·538 : 1·48. Three fits from 9 a.m. to 11 a.m. Blood 11.30 a.m. alkalinity 1·0387. Blood 12 noon alkalinity 1·26. Blood 2 p.m. alkalinity 1·43. Blood 5 p.m. alkalinity 1·538. Blood 10 p.m. alkalinity 1·538.

Case 25.—Aged 26, admitted October 19, 1893. Duration of epilepsy, six years. Bodily condition fair.

Family history.—Father and mother alive and healthy. No history of insanity, epilepsy, or phthisis.

Mental condition.—Is simple and childish in manner, incoherent in his remarks, expresses delusions of persecution, says "people follow him about to shoot him"; after fits is violent and abusive.

History of fits.—Had his first fit six years ago. It was stated to be caused by a large piece of wood falling on his head. Grand mal; left eyelid twitches three minutes prior to the fit. Mental confusion lasts about four hours.

Record of fits from admission to December 31, 1901:—Day fits, 115; night fits, 411.

Interparoxysmal alkalinity, 1·538 : 1·43. Alkalinity during aura, 1·26. Alkalinity fifteen minutes after fit, 1·0387. Alka-

linity one hour after fit, 1·385. Alkalinity two hours after fit, 1·43. Alkalinity four hours after fit, 1·538. Alkalinity twelve hours after fit, 1·59.

Case 26.—Aged 21, admitted November 1, 1894. Duration of epilepsy, not known. Bodily condition fair; usually constipated. No family history obtained.

Mental condition.—Is simple and childish in manner and talk. After fits is irritable and quarrelsome, and develops delusions of persecution.

History of fits.—Patient says he has had fits since nine years old. Grand mal; aura two minutes prior to the fit, which he describes as a painful sensation in his right forearm. Mental confusion lasts about six hours.

Record of fits from admission to December 31, 1901:—Day fits, 378; night fits, 456.

Interparoxysmal alkalinity, 1·538 : 1·48. Alkalinity sixty seconds before a fit, 1·18. Alkalinity one hour after, 1·26. Alkalinity two hours after, 1·385. Alkalinity four hours after, 1·538. Alkalinity twelve hours after, 1·59.

Case 27.—Aged 26, admitted November 3, 1893. Duration of epilepsy thirteen years. Bodily condition fair. Palate high and arched. Is myopic.

Family history.—Father died of lead palsy, intemperate. Mother alive and healthy. Maternal grandfather died of phthisis.

Mental condition.—Is simple and childish in manner and talk; mental reaction slow. Intellect weak. Memory defective. After fits is troublesome, irritable, emotional and impulsive.

History of fits.—Had his first fit when 13 years of age. Had "brain fever" when 4. Grand mal. Epigastric aura. Mental confusion lasts about four hours.

Record of fits from admission to December 31, 1901. Day fits, 420; night fits, 121.

Interparoxysmal alkalinity 1·48; half an hour after two severe fits, alkalinity 1·0387; one hour after two severe fits, alkalinity 1·26; two hours after two severe fits, alkalinity 1·385; four hours after two severe fits, alkalinity 1·538; twelve hours after two severe fits, alkalinity 1·59.

Case 28.—Aged 24, admitted January 31, 1902. Duration of epilepsy three years. Bodily condition fair.

Family history. Father and mother alive and healthy. A brother insane, died at Hanwell Asylum seven years ago. One sister insane at Salisbury Asylum.

Mental condition.—Is simple and childish in manner and talk. Memory defective; is unable to give a coherent account of himself; after fits is very excited.

History of fits.—Developed his epilepsy when 21 years of age. Grand mal, no aura. Mental confusion lasts about five hours. He has had several strong fits since admission.

Interparoxysmal alkalinity, 1·538 : 1·48. Two strong fits 10 a.m. Blood 10·30 a.m. alkalinity 1.0387. Blood 11 a.m. alkalinity 1·26. Blood 1 p.m. alkalinity 1·43. Blood 5 p.m. alkalinity 1·538. Blood 8 p.m. alkalinity 1·538.

Case 29.—Aged 27, admitted October 14, 1899. Duration of epilepsy, twenty years. Bodily condition fair. Mitral disease. Usually constipated.

No family history obtained.

Mental condition.—Is dull and feeble-minded, mental reaction slow. Memory defective for recent events. After fits is restless and impulsive.

History of fits.—Had his first fit when 7 years of age, said to follow scarlet fever. Grand mal, no aura. Mental confusion lasts about four hours.

Record of fits from admission to December 31, 1901.—Day fits, 71; night fits, 225.

Interparoxysmal alkalinity 1·48 : 1·43. Strong fit 2 p.m. Blood 2.20 p.m. alkalinity 1·12. Blood 3 p.m. alkalinity 1·26. Blood 5 p.m. alkalinity 1·48. Blood 7 p.m. alkalinity 1·538.

Case 30.—Aged 44, admitted November 4, 1893. Duration of epilepsy, six years. Bodily condition good.

Family history.—Father and mother dead. Two uncles and grandfather died of phthisis.

Mental condition.—Is dull and feeble-minded. Memory much impaired, especially for recent events. After fits is irritable, grumbles much and says his food is poisoned.

History of fits.—Developed his epilepsy when 38 years of age Grand mal, no aura. Mental confusion lasts about five hours.

Record of fits from admission to December 31, 1901.—Day fits, 188; night fits, 219.

Interparoxysmal alkalinity, 1·48. Half an hour after two fits, alkalinity 1·0387; one hour after two fits, alkalinity 1·26; two hours after two fits, alkalinity 1·43; three hours after two fits, alkalinity 1·538; five hours after two fits, alkalinity 1·538; eight hours after two fits, alkalinity 1·59.

Case 31.—Aged 19, admitted October 12, 1893. Duration of epilepsy, ten years. Bodily condition good.

No family history obtained.

Mental condition.—Is very dull and feeble-minded, restless after fits, and expresses vague delusions of persecution. Memory very defective.

History of fits.—Grand mal. Mental confusion lasts about three hours.

Record of fits from admission to December 31, 1901.—Day fits, 348; night fits, 762.

Interparoxysmal alkalinity 1·538. Five fits from 7 a.m. to 10.30 a.m. Blood 11 a.m. alkalinity ·831. Blood 1 p.m. alkalinity 1·26. Blood 2 p.m. alkalinity 1·43. Blood 5 p.m. alkalinity 1·59. Blood 9.30 p.m. alkalinity 1·538.

Case 32.—Aged 44, admitted August 17, 1895. Duration of epilepsy, thirty years. Bodily condition fair; is usually constipated.

No family history obtained.

Mental condition.—Is dull and feeble-minded. Memory much impaired. After fits is troublesome, restless, and impulsive.

History of fits.—Has had fits for 30 years. Grand mal, taste aura. Mental confusion lasts about five hours.

Record of fits from admission to December 31, 1901.—Day fits, 691; night fits, 199.

Interparoxysmal alkalinity, 1·538 : 1·48. Two strong fits 9 a.m. Blood 9.30 a.m. alkalinity 1·18. Blood 11 a.m. alkalinity 1·43. Blood 1 p.m. alkalinity 1·48. Blood 3 p.m. alkalinity 1·59. Blood 7 p.m. alkalinity 1·59.

Case 33.—Aged 23, admitted February 19, 1896. Duration of epilepsy, seventeen years. Bodily condition fair, suffers from indigestion.

Family history.—Father dead, cause unknown. Mother dead, cause heart disease. Patient the only child.

Mental condition.—Is simple and childish in manner and talk; has some religious exaltation with mild excitement.

History of fits.—Had his first fit when six years of age; did not have another for ten years; since that time he has had them frequently. Grand mal, no aura. Mental confusion lasts three hours.

Record of fits from admission to December 31, 1901.—Day fits, 575; night fits, 208.

Interparoxysmal alkalinity, 1·48 : 1·43. One slight fit 2 p.m.

Blood 3 p.m. alkalinity 1·385. Blood 4 p.m. alkalinity 1·48. Blood 6 p.m. alkalinity 1·59. Blood 10 p.m. alkalinity 1.59.

Case 34.—Aged 40, admitted November 11, 1895. Duration of epilepsy, twenty-four years. Bodily condition fair; pupils irregular, left contracted.

No family history obtained.

Mental condition.—Is dull, confused, and simple-minded. Memory much impaired; has no idea of time; after fits is violent, hears voices, and chatters to them.

History of fits.—Had his first fit when sixteen years of age. Grand mal, no aura. Mental confusion lasts six hours.

Record of fits from admission to December 31, 1901.—Day fits, 77; night fits, 352.

Interparoxysmal alkalinity, 1·538 : 1·48. Three strong fits from 1 p.m. to 2.30 p.m. Blood 2.45 p.m. alkalinity 1·0387. Blood 4.30 p.m. alkalinity 1·385. Blood 6.30 p.m. alkalinity 1·59. Blood 10.30 p.m., alkalinity 1·538.

Case 35.—Aged 65, admitted February 1, 1898. Duration of epilepsy, ten years. Bodily condition fair. Arteries very atheromatous, albumen in urine. Has been in the army, and lived twelve years in India. Scar on penis. Scars on both groins.

No family history obtained.

Mental condition.—Is dull and feeble-minded, mental reaction slow. Memory much impaired; after fits is pugnacious, violent, and abusive.

History of fits.—Had his first fit ten years ago. Grand mal. Epigastric aura. Mental confusion lasts about four hours.

Record of fits from admission to December 31, 1901.—Day fits, 147; night fits, 190.

Interparoxysmal alkalinity, 1·662. Alkalinity during aura, 1·26. Slight fit 10 a.m. Blood 10.15 a.m. alkalinity 1.26. Blood 12 noon alkalinity 1·48. Blood 2 p.m. alkalinity 1·59. Blood 6 p.m. alkalinity 1·59.

Case 36.—Aged 54, admitted December 13, 1900. Duration of epilepsy, five years. Bodily condition fair. Mitral systolic bruit, arteries atheromatous.

No family history obtained.

Mental condition.—Is simple and childish in manner and talk. Memory much impaired both for recent and remote events. After fits is very troublesome, and rushes wildly about the ward.

History of fits.—Developed his epilepsy about five years ago;

a week prior to his admission he had four fits. Grand mal, no aura. Mental confusion lasts about five hours.

Record of fits from admission to December 31, 1901.—Day fits, 9; night fits, 11.

Interparoxysmal alkalinity, 1·662. Strong fit at 2 p.m. Blood 2.30 p.m. alkalinity 1·0387. Blood 3 p.m. alkalinity 1·26. Blood 5 p.m. alkalinity 1·538. Blood 7 p.m. alkalinity 1·59.

Patient was subjected to the suprarenal treatment for twenty-one days; the number of fits was increased, but his mental condition improved.

Case 37.—Aged 18, admitted February 14, 1902. Duration of epilepsy, four years. Bodily condition fair.

Family history.—Father and mother alive and healthy. Paternal aunt insane, died at Banstead Asylum.

Mental condition.—Is dull and simple-minded; mental reaction slow. Memory much impaired for recent events.

History of fits.—Had his first fit when 14 years of age. Grand mal, epigastric aura. Mental confusion lasts three hours. He has had several fits since admission, mostly nocturnal.

Interparoxysmal alkalinity, 1·48 : 1·43. Alkalinity during aura 1·18. One hour after fit, alkalinity 1·26; two hours after fit, alkalinity 1·385; four hours after fit, alkalinity 1·48; six hours after fit, alkalinity 1·538; twenty-four hours after fit, alkalinity 1·59.

Case 38.—Aged 34, admitted May 18, 1900. Duration of epilepsy, seventeen years. Bodily condition fair; is usually constipated and suffers from indigestion.

No family history obtained.

Mental condition.—Is dull and simple-minded. Memory much impaired, especially for recent events. After fits is restless, impulsive, and develops persecutory delusions.

History of fits.—Had his first fit when 17 years of age. Grand mal. Ocular aura about two minutes prior to the fit. Mental confusion lasts about four hours.

Record of fits from admission to December 31, 1901.—Day fits, 88; night fits, 35.

Interparoxysmal alkalinity, 1·538 : 1·43. Alkalinity during aura 1·26. Fit 4 p.m. Blood 4.15 p.m. alkalinity 1·12. Blood 5 p.m. alkalinity 1·26. Blood 7 p.m. alkalinity 1·43. Blood 11 p.m. alkalinity 1.48.

Case 39.—Aged 44, admitted May 29, 1899. Duration of epilepsy not known. Bodily condition fair.

No family history obtained.

Mental condition.—Is dull and feeble-minded. Memory very defective, has no idea of time. After fits is excited, impulsive and very fond of making accusations against the attendant.

History of fits.—Grand mal, epigastric aura. Mental confusion lasts about six hours.

Record of fits from admission to December 31, 1901. Day fits, 104; night fits, 134.

Interparoxysmal alkalinity, 1·48 : 1·43. Strong fit, 1 p.m. Blood 1.20 p.m. alkalinity 1·0387. Blood 3 p.m. alkalinity 1·385. Blood 4 p.m. alkalinity 1·48. Blood 8 p.m. alkalinity 1·538. Blood 1 a.m. alkalinity 1·538.

Case 40.—Aged 28, admitted October 25, 1893. Duration of epilepsy, thirteen years. Bodily condition fair. Suffers from indigestion, frequently constipated.

Family history.—Father alive and healthy. Mother alive, very simple and eccentric. Mother's brother died in an asylum. Patient the only child.

Mental condition.—Is very simple and childish in manner and talk, and dirty in his habits. Memory very defective; after fits is restless and intractable.

History of fits.—Developed his epilepsy when 5 years of age. Grand mal. Mental confusion lasts about three hours.

Record of fits from admission to December 31, 1901. Day fits, 490; night fits, 998.

Interparoxysmal alkalinity 1·538 : 1·48. Fit 10 a.m. Blood 11 a.m. alkalinity 1·26. Blood 1 p.m. alkalinity 1·48. Blood 3 p.m. alkalinity 1·538. Blood 5 p.m. alkalinity 1·538. Six fits—nocturnal—3 a.m. to 4.30 a.m. Blood 11 a.m. alkalinity 1·48. Blood 12 noon alkalinity 1·59. Blood 5 p.m. 1·538.

General Considerations.

These results show clearly and consistently that the alkalinity of the blood in epilepsy undergoes marked variations. These variations manifest themselves in a diminution.

I.—The average alkalinity during the interparoxysmal period is lower than the average of the control cases.

II.—There is a sudden and pronounced fall immediately prior to the onset of the fit.

III.—There is a further diminution after the fit is over.

I.—*The Interparoxysmal Diminution.*

All the cases studied showed this diminution with the exception of No. 35 and No. 36.

In these two cases the alkalinity was normal and varied within physiological limits. This is explained by the fact that they are senile cases with arterial degeneration and alcoholic histories, having developed their epilepsy after forty years of age, and are cases of symptomatic epilepsy.

The interparoxysmal diminution varied in several of the cases, and it was more marked in cases suffering from gastric catarrh and constipation, *e.g.*, Cases 3, 32, 37, &c. The diminution is progressive right up to the epileptic discharge, immediately prior to which there is a marked fall.

How to interpret this gradual and progressive diminution is a matter of some difficulty; the constancy of the diminution is so much in evidence that the possibility of accidental occurrence, from such concurrent diseases as anæmia, gout or rheumatism, in which the alkalinity is lowered, is ruled out (and this period in an epileptic's life is one of comparative health), and, on the other hand, the constancy with which the alkalinity is maintained within physiological limits in health is equally so well marked that the question naturally arises: What is the cause of the diminution?

(*a*) It may be explained by the gradual accumulation of toxines of an acid nature in the blood. It is interesting and instructive to note that the lowest values of alkalinity were obtained from cases suffering from gastric catarrh and constipation. Various alienists have drawn attention to the fact that gastric and intestinal troubles bear some relation to the epileptic attack, as under these conditions the fits are more frequent. Agostini (13) advanced the theory that the exciting cause is a toxin absorbed from the alimentary canal; by correcting these disorders he found much benefit, and considerable diminution in the number of fits. In gastric and intestinal catarrh there is a condition of hyperacidity both in the stomach and the intestines. The hyperacidity is due to the presence of the organic acids, lactic, acetic, and butyric acids. These acids are absorbed, pass into the circu-

lation, and diminish the alkalinity of the blood. The writer has on several occasions raised the alkalinity in these cases by giving hydrarg. subchlor. gr. 5 and an antacid mixture. There is ample evidence to show that the alimentary canal is a fruitful source of toxines, which are absorbed into the blood, and by reacting on the organism bring forth abnormal manifestations of activity.

(*b*) It may be the result of deficient metabolism. The alkalinity of the blood is that of the body tissues generally, and the sum total of the metabolism of the body results in an alkaline reaction. Thus in epilepsy the general metabolism may be below par, with the result of a diminished value of the alkalinity of the blood, due either to a deficient amount of alkali or an excess of acid substances.

II.—*The Sudden and Pronounced Fall Immediately Prior to the Onset of the Fit.*

This phenomenon was observed in fifteen of the cases, and the blood was taken from ten seconds to two minutes before the fit. It may be regarded as the bio-chemical aura of the epileptic fit and a manifestation of some morbid change or changes taking place in the organism.

When the quantity of blood in the body (one-twelfth to one-fourteenth of the body weight), is taken into consideration, the amount of acid required to diminish the alkalinity must be relatively great, also the particular source or sources of the acid products must be qualitatively or quantitatively active. The most likely origin of these acid products are (*a*) *neuronic*; (*b*) *muscular*.

(*a*) *The neuronic origin.*—The neurones, like other cells in the body, undergo metabolic activity, and their functional activity depends upon a chemical change, a disintegration of food into chemical end products—carbonic and sarcolactic acids. The amount of acid formed must be infinitesimal; it is a case of the most highly developed cells evolving the maximum of work with the minimum formation of waste products.

The explanation of the sudden diminution by the acid

products of neurone metabolism seems very fallacious. The neurones concerned in an epileptic seizure are those of the Rolandic area—a cubic inch at most on either side—and the acid products formed by their activity cannot be sufficient to lower the alkalinity of a gallon of blood, which means an enormous quantity of acid. It requires 1·662 grammes of H_2SO_4 to neutralise the alkalinity of 1,000 cc. of blood serum, and in order to neutralise the alkalinity of the total amount of blood serum, requires roughly about 4 grammes of H_2SO_4—in fact, it seems very improbable that all the cells of the cerebral cortex, say 20 grammes, can produce acid substances equal to 4 grammes of H_2SO_4. The acid products of neurone metabolism are much weaker, consequently the amount would have to be greater. On this calculation it is impossible for the neurones to produce such an amount of acid from so small a source.

Further, if this diminution in the alkalinity is due to these neuronic chemical end products, what is the condition of affairs with regard to the cerebro-spinal fluid? Compared with the volume of the blood it is scanty (the amount present is about two ounces), and the reaction would therefore necessarily be acid. But an acid medium is incompatible with the life of the neurone. The immediate surroundings are alkaline, the cerebro-spinal fluid which bathes and comes into such close contact with the neurones is alkaline, the blood is alkaline, the neurones themselves have an alkaline reaction, the sea in which they live is alkaline, and the river which flows into the sea has an alkaline reaction. This suggests that for physiological neuronic activity an alkaline medium is essential. Even an excessive, abnormal, or disordered cerebral metabolism will not account for the production of this diminution directly, and for the above reasons the neuronic origin of the sudden drop cannot be maintained.

(*b*) *The muscular origin.*—The most important metabolic tissues in the body are the muscular and the glandular. Of the two, the former is the more active; this is so because it is the most abundant, and forms about 42 per cent. of the body weight. The muscles produce by

their activity the greater part of the body heat. Even during relative repose such as sleep the muscles are the seat of chemical changes, and produce a sufficient amount of heat to keep up the body temperature; also in functional paralyses where the metabolic processes in the muscles are not impaired by organic disease and the afferent and efferent channels are intact the nutrition of the muscles is relatively little impaired. The metabolism of the muscular tissue is under the control of the nervous system, and when the nervous system fails muscular metabolism is interfered with and the body temperature falls.

What has been stated above with reference to the production of heat, may be equally affirmed regarding the production of the chemical end products of muscular metabolism.

The preliminary chemical change is an oxidation, resulting in the formation of *inogen*, and the muscular contraction is a consequence of the disruption of this *inogen*, which is the first event in the response of a muscle to stimulation. It is a debatable point whether this chemical change is directly transformed into the mechanical energy which manifests itself in the muscular contraction. The large bulk of muscle engaged in the violent convulsions of an epileptic seizure is an ample source for the altered reaction of the blood. That the major part of the fall should occur before the visible and violent spasms of the convulsions appear, is consequently explicable on the following considerations:—

(I.) The muscles normally, even when at rest, are the seat of metabolic activity, and produce the bulk of the body heat.

(II.) During violent exercise, the extra amount of heat produced is only a proportion of the amount of heat required to keep the body temperature within normal limits.

(III.) The chemical change is the forerunner of the muscular contraction.

(IV.) The sensori-motor areas of the cerebral cortex control the metabolism of the muscles, as is evidenced by functional paralyses, muscular tonus, and section of the spinal cord with a consequent fall in the body temperature.

It is therefore probable that there is a considerable alteration in the metabolism of the cerebral neurones, with

consequent hyperexcitability and decreased inhibition some time prior to the actual epileptic discharge. This modified cortical activity brings about an increase of the metabolism which occurs prior to the visible spasms, and accounts for the sudden and pronounced diminution during this period.

III.—*The Further Diminution after the Fit is over.*

This diminution is well marked and was found in all the cases except after petit mal seizures. It is apparent soon after the fit is over, three to ten minutes, and lasts for some hours; the alkalinity gradually rises, the rise being more marked in the first hour. The return to normal varies in the different cases, but on an average takes from four to five hours. The explanation of this diminution is not far to seek. It is directly due to the acid products of muscular metabolism—carbonic and sarcolactic acids—generated during the violent tonic and clonic spasms of the muscles during the epileptic paroxysm. This phenomenon is physiological, and is seen, though in a less degree, after severe muscular exercise. The variations met with in the different cases depend upon the frequency and the number of the fits, and on the duration and the severity of the muscular twitchings. Thus, after one slight fit, the fall in alkalinity is 6°; after four fits, 8, 9 or 10°. Then again, this diminution is negligeable in cases of petit mal. These facts, together with the appearance of the fall after the spasms are over, and the gradual rise to the normal, seem to prove that the whole diminution is muscular in origin.

The relation of the diminution to the number of fits and to the duration and severity of the muscular contractions, holds good to a certain point, but the writer has taken blood from a patient who had forty fits in the short space of an hour, and from another patient after five fits, and has found the alkalinity to be of the same value, *e.g.*, ·6925. This points to a limit in the diminution.

The rapidity of return of the alkalinity to normal varies in the different cases, and in some cases, Nos. 3 and 4, the return was quick. Certain facts observed in these cases may account for the quick recovery: (*a*) free voiding of

urine; (*b*) free perspiration; (*c*) leucocytosis—the greater the leucocytosis the sooner the recovery. The ultimate end of these acid products may be accounted for by excretion. They may be destroyed by the increased number of leucocytes, or they may be used as food by some of the other tissues, or neutralised by the secretions of the glands. It was also observed that the return to normal bears a relation to the mental confusion of the patient after the attack: in Case 3, where the return to normal alkalinity is comparatively rapid, the mental recovery is also rapid; in Case 1, whose mental recovery is slow, the alkalinity keeps at a low value.

The effect of drugs upon the alkalinity is transient, and it is impossible to elevate and maintain the alkalinity within physiological limits for any appreciable length of time. The bromides elevate the alkalinity even to the normal of the control cases for a certain time, but on continued administration, and even when the dose is increased, the alkalinity falls. The best results were obtained from strontii bromidi, sodii bicarb. aa. gr. 15 *ter in die*; for some time the alkalinity was maintained at a high value, but only to fall again.

In the case of No. 3, a rectal enema of potas. brom. gr. 30, chloral hydratis. gr. 20, given after twenty-four fits, raised the alkalinity from ·831 to 1·385. This was maintained for forty-five minutes, after which it dropped again to 1·0387, and gradually attained its normal value in four hours.

Suprarenal extract has apparently little effect upon the alkalinity. The effect upon the mental state was good, and all the patients subjected to the treatment recovered from their mental confusion much sooner. One of the cases, No. 4, improved considerably; usually after a fit he has a headache for some hours, but when taking suprarenal he did not have headaches. In all the cases the number and frequency of the fits were much increased, and on this account the treatment was stopped. These results are very different to those obtained by Dr. Hill (14).

The exact *rôle* which a diminution in the alkalinity of the blood plays in the production of the epileptic attack is difficult to estimate. It is of the utmost importance for any

cell in the body to have a proper, adequate, and pure supply of blood, and this applies especially to the cerebral neurones, as they are extremely sensitive to a change in environment. This is well seen in the case of toxic agents circulating in the blood. As has been stated before, the conditions under which the neurones functionate is one of alkalinity, and it does not seem strange that any appreciable diminution in the alkalinity of their surroundings may bring about abnormal manifestations of activity. This applies with greater force in the case of the unstable, readily explosive, epileptic neurones. The writer has obtained good results in the treatment of epilepsy by maintaining the alkalinity of the blood within physiological limits; by doing so the number of fits is much diminished. Unfortunately it is impossible to elevate and maintain the alkalinity by the administration of drugs.

The Leucocytes.

I.—*The Interparoxysmal Period.*

There is a wide variation in the number of leucocytes. In some cases, the leucocytes were found to drop some hours before a fit. In other cases, the leucocyte count was low during the interparoxysmal period. These were cases who had frequent fits. In others, and these constituted the majority, there was a gradual drop right up to the paroxysm. A probable deduction is that the number and the activity of leucocytes depend upon the health of the epileptic in this period, that as the alkalinity of the blood diminishes and the nearer the patient is to his paroxysm, the lower is the leucocyte count, and the less the activity.

II.—*After the Fit.*

There is a distinct leucocytosis which shows itself a short time after the fit, and gradually increases, attaining its maximum from about fifty to seventy minutes after. The increase is due to the large and small hyaline cells. In the analysis of the leucocytes, the polymorphonuclear cells are diminished. The large hyaline cells are increased. The small hyaline cells are much increased. The eosinophiles are increased from two to ten hours after the attack.

The leucocytosis in the status epilepticus is not so constant, and is subject to wide variations. It takes a longer time to appear and is not so pronounced as after one individual fit. In one case, 45,000 leucocytes were counted after two fits. In another, 30,000 were counted after thirty fits in quick succession. In another case of status 12,000 white cells were counted after eighty-five fits.

The leucocytosis passes off gradually and undergoes the changes described under the interparoxysmal period. With regard to the causation, the consensus of experimental evidence seems to show that leucocytosis is to be looked upon as the reaction produced by a chemical substance circulating in the blood, and has its special mission to perform, *e.g.*, the removal or destruction of these substances. On this hypothesis, the leucocytosis following the epileptic fit may be explained. The increase of the eosinophiles some hours after the attack is much in evidence, and is also very constant, and it is probable that these cells complete the destruction of the waste products by means of their secretory functions.

Conclusions.

(1) The alkalinity of the blood in the interparoxysmal period is lower than the average of the control cases.

(2) The diminution is gradual and progressive, and is more marked in those cases suffering from gastric catarrh and constipation.

(3) There is a marked sudden and pronounced fall immediately prior to the onset of the fit.

(4) There is a further fall in the alkalinity after the fit is over; this diminution is seen from three to ten minutes after the attack.

(5) This after-diminution depends upon the duration and severity of the muscular twitching, and upon the degree of the alkalinity in the interparoxysmal period.

(6) There is a gradual return of the blood to its normal alkalinity, which takes place in five to six hours, the rise being more marked in the first hour.

(7) If the alkalinity keeps at a low value, it may determine the onset of another fit.

(8) The diminution after the fit is due to the chemical end products of muscular metabolism, *i.e.*, sarcolactic and carbonic acids, and not to substances in direct relation to the epilepsy.

(9) The diminution after a nocturnal fit takes a longer time to return to the normal than the diminution after a day fit.

(10) It is impossible to elevate and maintain the alkalinity within physiological limits for any appreciable length of time by the administration of drugs.

(11) There is a leucocytosis after a fit. The increase is due to the small hyaline cells, also to a less extent to the large hyaline cells. The polymorphonuclear cells are diminished. There is an increase in the eosinophile cells some hours after the attack.

(12) The leucocytosis is not so pronounced in status epilepticus; it diminishes with each seizure.

TABLE I.

Alkalinity of the Control Cases.

Case.	Occupation.	Alkalinity.	Alkalinity.
1. J. C.	Dispenser	1·662	1·662
2. W. E.	Head Attendant	1·662	1·662
3. J. D.	Attendant	1·662	1·59
4. W. B.	Attendant	1·731	1·662
5. A. E. P.	Clerk	1·662	1·662
6. W. O.	Porter	1·662	1·662
7. W. H.	Porter	1·662	1·662
8. W. H. F.	Physician	1·806	1·806
9. A. B.	Head Attendant	1·59	1·662
10. R. P.	Physician	1·662	1·662
11. E. F.	Physician	1·59	1·59
12. J. N.	Attendant	1·731	1·662
13. A. H. S.	Physician	1·662	1·59
14. J. A.	Attendant	1·662	1·731
15. W. C.	Clerk	1·662	1·731
16. B. A.	Engineer	1·662	1·662
17. J. L.	Attendant	1·662	1·662
18. W. A.	Attendant	1·662	1·662
19. J. B.	Clerk	1·662	1·662
20. A. C. B.	Attendant	1·662	1·662

Table showing the Alkalinity during the Aura and Varying Periods after Paroxysm.

	Aura.	10-30 Minutes.	1 Hour.	2 Hours.	3 Hours.	4 Hours.	5-12 Hours.	12-24 Hours.
Case 1, 7 fits ..	—	1·0387	1·26	1·385	1·43	—	—	1·43
,, 5 fits ..	—	—	1·18	—	1·43	1·48	1·48	—
,, 5 fits ..	—	·831	1·12	1·385	—	—	1·43	1·48
,, 1 fit ..	1·26	1·18	1·385	1·43	—	1·538	—	—
,, 2, 1 fit ..	—	—	—	—	1·385	—	1·538	—
,, 2 fits ..	—	—	1·26	1·385	1·48	—	1·59	—
,, 1 fit ..	1·26	1·18	1·385	1·43	—	1·538	—	—
,, 3, 8 fits ..	—	·831	1·26	1·385	—	1·48	—	—
,, 10 fits ..	—	1·18	1·385	1·26	—	1·48	—	—
,, 15 fits ..	—	·831	1·26	—	—	—	—	1·538
,, 4, 1 fit ..	—	1·0387	1·26	1·43	—	—	1·538	—
,, 5, 5 fits ..	—	·831	1·26	1·385	—	1·48	—	1·662
,, 1 fit ..	1·26	—	—	—	—	—	—	—
,, 6, 2 fits ..	—	1·0387	1·26	1·43	—	—	1·538	—
,, 7, 1 fit ..	—	1·18	1·26	—	—	—	—	—
,, 1 fit ..	—	1·0387	1·26	—	1·43	—	1·538	—
,, 8, 1 fit ..	—	1·12	1·385	1·48	—	1·538	—	—
,, 9, 1 fit ..	1·26	1·18	1·385	1·43	—	—	1·538	—
,, 10, 1 fit ..	—	—	—	—	1·385	—	1·538	—
,, 1 fit ..	—	1·12	—	1·385	—	—	1·538	—
,, 2 fits ..	—	·831	1·12	1·26	—	1·48	—	—
,, 11, 1 fit ..	1·385	1·18	1·385	1·48	—	1·538	—	—
,, 12, 1 fit ..	—	1·385	—	1·48	1·538	—	—	—
,, 3 fits ..	—	·831	1·12	1·26	—	1·43	1·48	—
,, 13, 2 fits ..	—	1·12	1·26	—	1·43	1·48	—	—
,, 14, 4 fits ..	1·385	1·12	—	1·385	—	1·48	1·59	—
,, 15, 1 fit ..	—	1·26	1·385	1·48	—	1·59	—	—
,, 16, 3 fits ..	—	1·12	1·26	—	1·48	—	1·59	1·59
,, 17, 2 fits ..	—	1·0387	—	1·385	1·48	—	1·59	—
,, 18, 1 fit ..	—	—	1·26	1·385	—	1·48	1·59	—
,, 19, 1 fit ..	—	—	1·385	1·43	—	1·48	1·59	—
,, 20, 2 fits ..	—	1·0387	1·26	1·43	—	1·59	—	1·59
,, 21, 1 fit ..	—	1·12	1·26	1·385	—	—	—	1·538
,, 22, 2 fits ..	—	1·12	—	1·43	—	1·43	1·59	—
,, 23, 1 fit ..	1·26	1·18	1·26	—	1·43	—	1·59	—
,, 24, 3 fits ..	—	1·0387	1·26	—	1·43	—	1·538	—
,, 25, 1 fit ..	1·26	1·0387	1·385	1·43	—	1·538	—	1·59
,, 26, 1 fit ..	1·18	—	1·26	1·385	—	1·538	—	1·59
,, 27, 2 fits ..	—	1·0387	1·26	1·385	—	1·538	—	1·59
,, 28, 2 fits ..	—	1·0387	1·26	—	1·43	—	1·538	—
,, 29, 1 fit ..	—	1·12	1·26	—	1·48	—	1·538	—
,, 30, 2 fits ..	—	1·0387	1·26	1·43	1·538	—	1·538	—
,, 31, 5 fits ..	—	·831	1·26	1·43	—	—	1·59	1·538
,, 32, 2 fits ..	—	1·18	—	1·43	—	1·48	1·59	—
,, 33, 1 fit ..	—	—	1·385	1·48	—	1·59	1·59	—
,, 34, 3 fits ..	—	1·0387	—	1·385	—	1·59	1·538	—
,, 35, 1 fit ..	—	1·26	—	1·48	—	1·59	1·59	—
,, 36, 1 fit ..	—	1·0387	1·26	—	1·538	—	1·59	—
,, 37, 1 fit ..	1·18	—	1·26	1·385	—	1·48	1·538	1·59
,, 38, 1 fit ..	1·26	1·12	1·26	—	1·43	—	1·48	—
,, 39, 1 fit ..	—	1·0387	—	1·385	1·48	—	1·538	—
,, 40, 1 fit ..	—	—	1·26	—	1·48	—	1·538	—
,, 6 fits ..	—	—	—	—	—	—	1·48	1·59

Cases.	Leucocytes.	Polymorphs.	Large Hyaline.	Small Hyaline.	Eosinophile.	
		p.c.	p.c.	p.c.	p.c.	
Case 1 ..	9,500	65	6	25	3	Interparoxysmal period.
,, ..	11,000	68	5	23	4	10 minutes after 7 fits.
,, ..	21,000	60	8	29	5	60 minutes after 7 fits.
,, 2 ..	14,000	60	11	25	4	60 minutes after 1 fit.
,, 3 ..	9,200	68	7	22	3	Interparoxysmal period.
,, ..	19,000	60	8	30	2	40 minutes after 8 fits.
,, 4 ..	10,000	70	6	21	3	Interparoxysmal period.
,, ..	12,000	62	4	30	5	4 hours after 1 fit.
,, 5 ..	11,000	70	7	18	5	12 hours after 5 fits.
,, 6 ..	18,000	58	8	33	2	60 minutes after 2 fits.
,, 7 ..	19,000	59	9	30	3	50 minutes after 1 fit.
,, 8 ..	17,000	60	10	29	1	40 minutes after 2 fits.
,, 9 ..	12,400	68	6	23	3	80 minutes after 1 fit.
,, 10 ..	14,000	60	8	30	3	50 minutes after 2 fits.
,, 11 ..	9,000	70	7	20	3	12 hours after 1 fit.
,, 12 ..	23,000	58	8	32	3	1 hour after 3 fits.
,, 13 ..	20,000	58	6	39	2	1½ hours after 1 fit.
,, 14 ..	11,000	61	6	25	8	6 hours after 4 fits.
,, 15 ..	9,000	70	4	23	3	24 hours after 2 fits.
,, 16 ..	8,000	62	6	23	9	8 hours after 1 fit.
,, 17 ..	12,000	56	7	32	5	3 days after 1 fit.
,, 18 ..	13,000	52	7	38	3	3 hours after 2 fits.
,, 19 ..	9,000	68	8	20	4	4 days after 1 fit.
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References.

(1) Luntz. *Centralblatt für die Medicinischen Wissenschaften*, 1867.
(2) Lassar. *Archiv. fur die gessammte Physiologie*, Band xviii.
(3) Leibrich. "Berichte der Deutschen Chemischen Gesellschaft Bl.," p. 48, 1869.
(4) Landois. "Rial Encyclopedie," iii., p. 161, 1885.
(5) Clifford Allbutt. "System of Medicine," vol. v., p. 448.
(6) *Lancet*, vol. ii., 1897, p. 719.
(7) "Schäfer's Physiology," vol. i., p. 719.
(8) Charon et Biche. *Archives de Neurologie*, 1897, p. 24.
(9) Lui. *Revista sper de Freniatria*, 1898, p. 1.
(10) Clifford Allbutt, vol. v., p. 416.
(11) Rutherford Macphail. "Hack Tuke's Dictionary of Psychological Medicine," Diseases of the Blood.
(12) Kroumbmiller. *Revue de Medicine*, 1898.
13) Agostini. *Revista Sper de Freniatria*, 1896.
(14) Hill. *Bulletin of the Laboratory of Mount Hope Retreat*, 1899, p. 49.

Reviews.

Traité des Maladies de la Moelle Epinière. Par J. Dejerine, Professeur a la Faculté de Médecine de Paris, Médecin de l'Hospice de la Salpêtrière, et André Thomas, ancien interne des Hopitaux de Paris, 1902.

This work commences with a description of the normal anatomy and physiology of the cord. The authors commit themselves definitely to the neurone theory at the outset, and, though constrained to admit that recent research has tended to throw doubts upon its unqualified acceptance, they still cling to it, partly because of the simplicity of its conception, partly on histological and pathological grounds. It might, however, be pointed out that the latter evidence is perhaps not so "irrefutable" as the authors would have us suppose.

Their description of the anatomy of the cord is somewhat disappointing; thus, for example, in describing the endogenous fibres of the posterior columns it is stated that the descending peripheral zone of Hoche and the "comma" tract of Schulze are two anatomically independent bundles of which the former alone is continued downwards as the "oval field" of Flechsig and the "triangle" of Gombault and Phillippe. Such a view, however, is not by any means universally accepted, and there are good grounds for preferring to believe that all the descending endogenous tracts in the posterior columns form one continuous system. The "septo-marginal" part of this system is not mentioned. The authors are much less dogmatic in their views as to the origin of the fibres of Gowers' tract, which, according to them, may be from the posterior, the lateral or the anterior horn. The latter group is now generally accepted as the probable source. To designate Monakow's bundle as the "faisceau pre-pyramidal (Thomas)" is surely to place an unnecessary restriction on its area, since it has been clearly shown to overlap to a considerable extent the lateral pyramidal tract. The antero-lateral descending fibres are all grouped together in a somewhat wholesale fashion, and a rather insufficient account is

given of these various tracts, amongst which, for example, might have been mentioned the ventral longitudinal bundle along the ventral border of the anterior median fissure, the ponto-spinal tract or "Fissuren-strang," the vestibulo-spinal tract from Deiters' nucleus, Helweg's "Dreikantenbahn" and others.

An interesting section is that which deals with the general pathology of cord diseases. The chief etiological factors are briefly summarised as four in number:—heredity, infection, intoxication and traumatism. Before passing to the individual diseases of the cord, a section is devoted to spinal symptomatology in general. On the much disputed point as to the condition of the tendon reflexes in total transverse lesions of the cord, the authors maintain that permanent flaccid paraplegia with loss of tendon reflexes is a certain sign of complete division of the cord, spastic paralysis with increased reflexes being characteristic of an incomplete lesion. In the investigation of sensory phenomena, a good account is given of the mode of examination of the osseous sensibility, a form of sensation consisting in the vibration perceived when the base of a vibrating tuning-fork is placed on a bony surface (Egger). This feeling is apparently due to stimulation of the periosteum without intervention of the skin. Osseous anæsthesia is met with in tabes, in syringomyelia, in Brown-Sequard's paralysis (on the side of the motor paralysis), in myelitis, and, to a certain degree, in hemiplegia of cerebral origin. It is interesting to note that the normal flexor plantar reflex is considered to be a reflex of the cerebral cortex, Babinski's extensor reflex being regarded, not as a mere modification of the flexor response, but as an entirely fresh phenomenon of spinal origin. The micturition centre is still located by the authors in the conus medullaris. A considerable amount of evidence, however, has recently been brought forward by Müller[1] of Erlangen and others, indicating that the striped muscle of the neck of the bladder is alone under direct control of the cord, and that the centre for the bladder wall is located outside the central nervous system in the hypogastric plexus of the sympathetic.

The classification of affections of the spinal cord adopted by Dejerine and Thomas has the merit of simplicity. Diseases of the cord are divided into secondary and primary. The secondary affections comprise traumatism, slow compression, and the cord affections supervening in Pott's disease. Primary affections are subdivided into systematised and non-systematised. Systematised diseases comprise chronic anterior poliomyelitis, amyotrophic

[1] *Deutsche Zeitsch. für Nervenheilkunde*, 1901, Band 21, pp. 86-154.

lateral sclerosis, tabes, Friedreich's ataxia, combined sclerosis and spastic family paraplegia. The non-systematised are again subdivided into two groups:—one group, of toxo-infectious nature, includes acute myelitis, acute and subacute anterior poliomyelitis, Landry's paralysis, and abscess of the cord; the other group, whose nature is less definitely understood, includes multiple sclerosis, hæmatomyelia, hydromyelia and syringomyelia, tumours of the cord, and, curiously enough, Little's disease.

The individual diseases are then considered in detail, and a clear account is given of the pathology, symptoms, and diagnosis of each. The authors regard most cases of "railway spine" as examples of traumatic hysteria, a certain proportion being cases of true spinal concussion. No rules, however, are laid down whereby those two can be differentiated. Attention is specially directed to post-traumatic organic affections of the cord, and it is pointed out how in certain cases a traumatism may rouse a latent predisposition, for example, to tabes, or give a point of attack for microbic infection, for new growths, or for some systemic degeneration.

The authors maintain, in opposition to Leyden and others, that chronic anterior poliomyelitis does occasionally occur independently of sclerosis of the lateral columns, and they adduce pathological evidence in support of their view. But they admit that the vast majority of cases of so-called progressive muscular atrophy are associated with changes in the lateral white columns, and should rather be classed as amyotrophic lateral sclerosis. The latter affection is one which tends to spread upwards and cause bulbar paralysis, whereas pure anterior chronic poliomyelitis is a much rarer and slower disease, which does not attack the bulbar nuclei.

In an otherwise excellent description of disseminated sclerosis it is curious to find no reference to those transient palsies of functional type which are so frequently to be observed in the early stages of the disease, and to which considerable attention has been drawn, especially by English writers.

An interesting account is given of the pathological anatomy of cavities in the cord, and examples are described both of syringomyelia proper, where the pathological cavity is distinct from the central canal, and of the rarer hydromyelia, where the central canal is itself dilated. The occasional occurrence of small neuromata in the substance of a syringomyelic cord, little nodules of interlaced young nerve-fibres, commonly in the anterior part of the cord, is emphasised, but their significance is as yet obscure.

The authors, whilst admitting that Little's disease is usually due to a bilateral cerebral lesion, maintain that the disease may also be due to a primary lesion of the cord. The reasons for this somewhat startling statement, it must be confessed, are far from convincing. Their contention is based on a single case in which a focal lesion was found in the upper cervical region, implicating the posterior cornua and the intervening posterior columns, and even in that case they figure degeneration of the pyramidal tracts above the level of the spinal lesion.

The longest section in the book is devoted to the discussion of tabes. Syphilis is regarded as its primary cause, other factors, such as nervous heredity, exposure to cold, excesses, trauma, fatigue, &c., being of secondary importance. The signs and symptoms of the disease are described in great detail, and various theories as to the nature of the underlying pathological process are discussed. The conclusion at which the authors arrive is that tabes is essentially a degenerative disease of the exogenous posterior column fibres. Why the intramedullary extent of the posterior root fibres should be so severely attacked, why the affection of the posterior roots should be so marked close outside the cord and so rapidly diminishing in intensity as the ganglion is approached, and most difficult of all, why the cells of the root ganglion itself should be practically unaffected, are questions which the authors confess themselves unable to answer.

The cord changes in pernicious anæmia are referred to as a form of "pseudo-tabes," a term which seems somewhat inadequate in view of the widespread extent of the cord degenerations that are found. No account is given of the striking clinical picture afforded by cases of acute combined sclerosis, with its characteristic sudden changes in symptomatology as the disease progresses.

The work as a whole is an excellent example of current neurological teaching in France, and well repays perusal.

PURVES STEWART.

The Treatment of Tabetic Ataxia. By Dr. H. S. FRENKEL. English edition, translated and edited by L. FREYBERGER, M.D.

DR. FREYBERGER prefaces this English edition with the information that it is not a translation, but that the language of the original has been as closely followed as is consistent with a clear exposition of the author's meaning. Whilst the desired result has, on the whole, been attained with a fair amount of success, many sentences, especially in the theoretical part of the work, remain nearly as much involved as if they had been literally translated from the German.

The detailed description of the treatment is very clearly given, and, with the help of the very numerous illustrations, should enable not only the physician but the nurse to carry out all the directions of the author with precision and intelligence.

The theory upon which Frenkel's treatment of ataxy is based assumes that the incoordination of tabes dorsalis is due to the diminution or loss of the normal sensory impulses which reach the central nervous system from the muscles, tendons and joints, and it is contended that this want can be to a large extent compensated for by the habitual use of visual impulses in place of those which are lost. This theoretical consideration is well supported by practical results, and it is now admitted by those who have utilised this system that the re-education of tabetics in movements of their limbs and trunk, under skilled supervision, can produce in suitable cases an amelioration of coordination which is unattainable by any other therapeutical measure.

Dr. Freyberger's work will have served a very useful purpose if it brings the profession in this country to recognise this fact more clearly than has hitherto been the case.

E. FARQUHAR BUZZARD.

PROCEEDINGS OF THE NEUROLOGICAL SOCIETY OF LONDON.

At a Meeting held at the Physiological Laboratory, University College, on December 4, at 8.30 p.m., the following communications were made :—

SIR VICTOR HORSLEY AND DR. BEEVOR.—*On the Pallio-tectal system of fibres* (*see* page 436).

DR. H. K. ANDERSON.—*On the part played by the dilatator in reflex pupillo-dilatation and in hippus, and on the alleged existence of irido-inhibitory fibres in the oculo-motor and cervical sympathetic nerves.*

After excision of a ciliary ganglion pupillo-dilatation was observed when light was re-admitted to the eye (the other eye being closed), if the exclusion of light was affected by a hand or cloth placed over the eye, but not if the illumination of the eye was varied without touching the animal. Light, therefore, cannot by itself vary the tone of either the sphincter or dilatator iridis through the cervical sympathetic nerve, though sensory stimulation can.

On the other hand, if a superior cervical ganglion be removed from a kitten 30 hours or more previously, the pupil on the side of the denervation may be larger than the control in dim light ("paradoxical pupillo-dilatation"), though smaller in bright light; this reversal of the difference between the two pupils (in the light of evidence that the strength of the sphincter is not affected by the denervation), must be attributed to the presence of relatively greater tone in the sound dilatator in bright light than in dim, when compared with the corresponding tone of the denervated dilatator.

This reversal of the difference between the two pupils might be affected by light causing relatively greater inhibition of the denervated dilatator through the oculo-motor nerve, but there is

evidence against this explanation, since, if the paradoxical pupillo-dilatation be accentuated, as it readily may, by excitement, the pupil on the side with the denervated dilatator will remain moderately dilated even in bright sunlight, although the control is at the same time small; moreover, though both pupils react meanwhile with equal readiness to light, the paradoxically dilated pupil may remain for more than two minutes after the excitement has ceased relatively larger than the control, the disappearance of the paradoxical dilatation being, so far as I could detect, not hastened by the more brilliant illumination of the eyes. There was, therefore, no evidence in these observations that the denervated dilatator could be inhibited through the oculo-motor nerve more than the sound dilatator, or that the dilatator could be inhibited at all in this way.

The relative increase of size in the pupil on the sound side in the observation given above must, therefore, be attributed to a relative increase of tone in the sound dilatator in bright light, which is presumably caused by the increased tension of the contracting sphincter exerting greater tension upon the corresponding dilatator, and so stimulating it as in the case of a tendon-phenomenon; and in this connection also it may be noted that the same reversal of the difference between the pupils does not occur if the control sympathetic nerve is cut.

My observations also suggest that hippus is caused by rhythmic activity of the centrum cilio spinale inferius of Budge, since after excision of the ciliary ganglion the initial dilatation which followed a sensory stimulus was followed by oscillations of the pupil, and rhythmic oscillations at intervals of about four seconds were several times observed for more than five minutes continuously without sensory stimulation. In this connection the observations of Förster, Schadow, Damsch and others are discussed.

J. Herbert Parsons.—*On the relationship of intracranial pressure to the ocular circulation* (*Preliminary communication*).

The experiments were performed upon dogs, and must not, without great caution, be held to apply to higher mammals, on account of the very different blood-supply of the eye. To obviate this difficulty as far as possible the external carotid was tied so that the eye was then only supplied by the internal carotid and the circle of Willis. The eye was used as a plethysmograph, the intraocular tension being recorded. The blood pressure was

recorded from the femoral artery. The animal was anæsthetised with morphia and A. C. E. mixture, and curare was given.

It was first shown that the ocular vessels act passively in all large changes of general blood pressure, so that the intraocular tension varies *pari passu* with the blood pressure. This was shown by tracings of compression of the aorta, stimulation of the vagus, vasomotor centre, splanchnics, &c., Traube-Hering curves, and drugs (nicotin, &c.).

The intracranial pressure was raised by utilising Hill's brain pressure gauge in various ways, *e.g.*, by forcing mercury into an indiarubber bag inside the cerebral cavity by saline pressure, by bleeding from the opposite carotid into the cranial cavity, &c. The curves obtained by stimulating the peripheral end of the vagus, and by drugs (nicotin, adrenalin, &c.), were compared before and after raising intracranial pressure. It was found that the change was minimal, even with pressures far above the blood pressure, and even with the opposite common carotid tied, as well as the external carotid of the same side.

Both vagi being cut, the animals usually survived with very high intracranial pressure, but the heart eventually gave out, owing to the high blood pressure induced through the stimulation of the vasomotor centre. As the blood pressure fell in these cases the intraocular tension rose enormously, probably due in part to the obstruction to venous outflow, but the exact reason of this phenomenon requires further investigation.

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EDITOR.

Explanatory Note.—In consequence of an error in the paging of Part II. of vol. xxv., it will be found that pages 257 to 356 occur twice, the first time in Part II. and the second time in Part III. In the Index of the volume, the letter *a* standing after a figure refers to that page in Part II. and the letter *b* to that page in Part III.

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AND

LIST OF OFFICE BEARERS AND MEMBERS

OF THE

Neurological Society of London,

1902,

WITH THE

Annual Report of Council, and Balance Sheet for the Year 1901.

LONDON:
JOHN BALE, SONS & DANIELSSON, LTD.
83-89, GREAT TITCHFIELD STREET, OXFORD STREET, W.
1902.

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Secretaries.

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Neurological Society of London.

DRAFT REPORT OF COUNCIL.

FEBRUARY 6, 1902.

The Council has much pleasure in reporting the steady increase in the Members, who now amount to 220—an increase of fifty in the last ten years. It has, however, to regret the loss, by death, of two members, Dr. LESLIE OGILVIE and Dr. HENRY SUTHERLAND.

It has also to lament the death of Dr. HUGHES BENNETT, who was compelled by ill-health to resign his membership a few years ago. In the early days of the Society Dr. HUGHES BENNETT was one of its most active and useful members; he was Secretary during the years 1886 and 1887, and Member of Council from 1888 to 1891.

The Presidential Address was given by Dr. MICKLE, who took for his subject "Mental Wandering." In June, on the invitation of Professor DRESCHFELD and other members living in Manchester, the Society held a meeting in that city—the third time it had met out of London. At the meeting most successful pathological, clinical, and experimental demonstrations were arranged and were attended by a very large number of members and visitors; and in the evening the Society was hospitably entertained to dinner by the Manchester members. The meeting was an unqualified success, and the Council desires to record its grateful thanks to all concerned, particularly to Mr. THORBURN, Professor STIRLING, Dr. JUDSON BURY and Dr. E. S. REYNOLDS, who formed the Reception Committee.

Under the Editorship of Dr. PERCY SMITH, "Brain," the organ of the Society, continues to hold a leading place among neurological publications. The cost of illustrating papers in "Brain" had of recent years been increasing to such an extent that it was absorbing most of the income of the Society. The Council has therefore been compelled to put a limit to the amount which can be paid by the Society for the illustration of each paper.

Chiefly owing to this increased expenditure in illustration, the resources of the Society have been somewhat strained. Bills for over seventy pounds for illustrations occurring during 1900 were not sent in to the Treasurer until

the present financial year. The payment of these bills leaves the finances of the Society at the end of this year in a state of temporary embarrassment, as is shown on the appended Balance Sheet; but, with retrenchment in expenditure, the Council believes that at the end of twelve months they will again be in a satisfactory condition. The Council proposes to increase the income of the Society by raising the annual subscription to a guinea instead of one pound.

In the Report for 1896 it was announced that Sir WILLIAM BROADBENT had generously given a grant of thirty-six guineas towards the expenses of preparing an Index of "Brain." The work was entrusted to a number of different workers, and the subjects indexed on cards. Owing to several unavoidable circumstances, the arrangement of these cards for the formation of the Index was delayed. Early in the present year the cards were handed to the present Editor for arrangement and publication, but owing to the want of any uniformity of plan on the part of the different indexers, the preparation of the Index for the press by Dr. PERCY SMITH has involved an immense amount of labour. The final proofs of the Index, which deals with the first twenty-three volumes of "Brain," *i.e.*, down to the end of 1900, have been corrected, and the volume will very shortly be issued by Messrs. Macmillan, from whom Members can obtain it at a reduced price. The Council desires once more to express its warmest thanks to Sir WILLIAM BROADBENT; and also to Dr. PERCY SMITH for the pains and care which he has taken to make the volume a useful work of reference to neurologists.

An abstract of the Proceedings of the Society appended to this Report shows the character and value of the work of the Society during the past year.

Proceedings of the Society during the year 1901.

February 14.—Dr. W. J. MICKLE, Inaugural Address, "Mental Wandering."

March 21.—Dr. F. E. BATTEN, "Four cases of congenital ataxia in children." Dr. FARQUHAR BUZZARD, "Atrophy of arms with anæsthesia over distribution of the first dorsal root." Dr. RISIEN RUSSELL, "Syringomyelia with Charcot-joint." Dr. W. A. MARRIS, "Two cases resembling disseminated sclerosis." Dr. STILL, "A case of paramyoclonus multiplex."

May 9.—Dr. JOHN TURNER, "A method of staining nervous tissues in methylene blue." Dr. MICHELL CLARKE, (1) "A case of pachymeningitis of the spinal cord"; (2) "Changes in the posterior columns of the spinal cord in a case of pernicious anæmia"; (3) "Tumour of the right optic thalamus." Dr. WAKELIN BARRATT, "Changes in the nervous system in a case of old-standing amputation." Dr. FREDERICK BATTEN, "Specimens from three cases of infantile paralysis."

June 22.—An extraordinary meeting of the Society was held at Manchester. *Specimens were shown by:* Dr. A. BRUCE, (1) Photogravures of each segment of the normal spinal cord; (2) Photographs and sections of—(*a*) Hæmorrhage into spinal cord, (*b*) Cavities in cord above a spina bifida, (*c*) Syringo-myelia, (*d*) Progressive muscular atrophy and amyotrophic lateral sclerosis, (*e*) Glioma of pons, (*f*) Syphilitic meningo-myelitis; (3) Photographs from a case of complete paralysis of the brachial plexus. Dr. JUDSON BURY, (1) Porencephalus; (2) Hydrocephalus; (3) Acromegaly. Professor SHERIDAN DELÉPINE, (1) Actinomycotic abscess of brain; (2) Experimental arsenical neuritis; (3) Other lesions of the central nervous system. Professor J. DRESCHFELD, (1) Spinal cord in ataxia paraplegia; (2) Spinal cord in disseminated myelitis; (3) Casts and photographs. Mr. W. MILLIGAN, (1) A portable surgical motor. Dr. F. CRAVEN MOORE, (1) Multiple gummata of brain and spinal cord; (2) Hæmorrhagic meningo-encephalitis (influenza) (Dr. DRESCHFELD's case); (3) Metatastic calcification of vastus internus tendon with Charcot's arthropathy (Dr. DRESCHFELD's case); (4) Specimens from poisoning by arsenical beer; (5) Cerebral tumours. Dr. F. W. MOTT, Effects of bitulin, abrin, absinthe, and picrotoxin upon nerve-cells. Drs. ORR and ROWS, (1) Types of nerve-cells in the spinal ganglia of rabbits; (2) Nerve-cells in the spinal ganglia of man and different forms of chromatolysis in general paralysis of the insane; (3) Spinal ganglion cells in acute mania,

showing vacuolation. Dr. E. S. Reynolds, Photographs of neurological cases, including a series illustrative of the recent epidemic of arsenical poisoning. Professor C. S. Sherrington and Dr. E. E. Laslett, Microscopical sections (*infra*). Professor W. Stirling, (1) Exhibits to illustrate some of the phenomena of stereoscopic vision; (2) An original experiment on binocular colour vision; (3) An experiment to show how the actual size of the pupil is affected by the cornea; (4) View of the interior of the frog's heart to show the arrangement of its muscular fibres; (5) Enucleation of the eyeball and removal of the floor of the orbital cavity, showing position of soft palate in phonation; (6) Simple method of examining the retina in a living rabbit; (7) A classical experiment concerning the discovery of the capillaries (Malpighi, de pulmonibus) and a modern one; (8) Some optical illusions; (9) Some experiments in physiological optics; (10) Lantern slides of some distinguished physiologists; (11) Original picture of the Kircher's "Experimentum Mirabile"; (12) Some anaglyphs; (13) The structure of some electrical organs; (14) Complete injection of the blood-vessels of the eyeball of a small animal. Dr. E. F. Trevelyan, (1) Various specimens showing the value and permanency of Laskowsky's method; (2) Specimens preserved in Kaiserling's fluid; (3) Tuberculous tumour of the brain, meninges and skull; (4) Intact pia-arachnoid from a fœtus. Professor A. H. Young, Stereoscopic photographs of the brain. Dr. W. B. Warrington, (1) Sections of unilateral optic atrophy; (2) Photographs of Tooth's peroneal atrophy. Dr. R. T. Williamson, (1) Two cerebellar tumours with photographs; (2) Microscopical specimens of—(*a*) Progressive muscular atrophy, (*b*) Early tabes, (*c*) Acute anterior poliomyelitis of the adult. (*d*) Myelitis in the distribution of the anterior and of the posterior spinal arteries, (*e*) Peripheral nerves in multiple neuritis, (*f*) Spinal syphilis—thrombosis, hæmorrhage and myelitis, (*g*) Retro-bulbar optic neuritis associated with cancer of stomach. *Clinical cases were shown by*: Dr. Ashby. Dr. Judson Bury, (1) Syringomyelia with hemianæsthesia; (2) Sensory aphasia (two cases); (3) Ophthalmoplegia; (4) Hemiplegia, hemianæsthesia and impairment of special senses on one side. (5) Cases of muscular atrophy; (6) Hæmorrhage (?) into the spinal cord. Dr. Dreschfeld (1) Thomsen's disease (two cases); (2) A family (five cases) showing various stages of Erb's muscular dystrophy. Dr. Haring. Dr. Harris, Unusual defect in the skull (? cephalhydrocele) with both hysterical and epileptic attacks. Dr. Dixon Mann. Dr. E. S. Reynolds, (1) Locomotor ataxia with multiple joint lesions; (2) Unilateral lesion of the spinal cord (two cases); (3) Ataxia paraplegia (disseminated sclerosis?); (4) Chronic anterior poliomyelitis. Dr. R. T. Williamson, (1) Unilateral tremor most marked in leg (? paralysis agitans); (2) Very early tabes with knee-jerks present (two cases); (3) Disseminated sclerosis following influenza. Dr. Williamson and Dr. P. Tytler, Hydatid of spine (extra-dural) with compression myelitis; operation with gradual improvement for twelve months. Professor C. S. Sherrington and Dr. E. E. Laslett gave a short "Note on the third, fourth and sixth cranial nerves." Drs. Alexander Bruce, Mott and Orr gave lantern demonstrations of specimens shown in the Histological Laboratory (*supra*). Professor Wm. Stirling showed (1) Some classical experiments bearing on neuro-physiology, and one new experiment; (2) Malapterurus electricus (living) and its mode of feeding.

October 31.—Dr. FERRIER, "Case of successful removal of a cerebellar tumour." Dr. FERRIER and Dr. ALDREN TURNER, "Case of successful removal of a cerebral tumour." Dr. ROBERT HUTCHISON, "Unilateral incoordination with inability to rotate the eyes downwards in a mentally defective boy." Dr. BEEVOR, "A case of affection of the first dorsal nerve." Dr. HEAD, (1) "A case of muscular atrophy in a young woman, probably of neuritic origin"; "A case for diagnosis." Dr. BATTEN, "Spasmodic movements in the limbs of an infant." Dr. MUSKENS demonstrated lantern slides to illustrate the segmental disturbances of sensation in cases of tabes dorsalis and epilepsy.

December 4 was devoted to psycho-physical methods, and Dr. RIVERS gave a demonstration (1) On methods for estimating mental fatigue and practice; (2) On methods of measuring mental illusions. Dr. F. SMITH showed an apparatus for measuring reaction time.

BALANCE SHEET, 1901.

Cr. NEUROLOGICAL SOCIETY. **Dr.**

Receipts.	£	s.	d.
To Balance	66	1	4
Subscriptions	230	5	6
Contributions by Authors to Illustrations in "Brain"	63	9	0
	£359	15	10

Expenditure.	£	s.	d.	£	s.	d.
By Stationery and Printing—						
Bale and Danielsson	30	12	7			
Pulman	0	10	6			
				31	3	1
Illustrations—May to September, 1900—						
Bale and Danielsson				67	14	6
,, October to February, 1901—						
Bale and Danielsson	78	1	6			
Typographic Etching Co.	9	11	8			
				87	13	2
,, Spring, Summer, Autumn Nos., 1901—						
Bale and Danielsson				124	14	6
Microscopes and Lantern—C. Baker	2	12	0			
A. Hawes	1	1	0			
				3	13	0
Hire of Rooms, and Refreshments—						
Medical Society				20	15	0
Hire of Examination Hall	5	5	0			
Meeting at Manchester	1	12	0			
				6	17	0
Petty Cash				1	0	0
Balance				16	5	7
				£359	15	10

Assets.	£	s.	d.
To Half-Share Profit on "Brain"	35	11	9
Contribution by Messrs. Macmillan towards cost of Illustrations in "Brain"	11	17	3
Balance at Bankers	16	5	7
	63	14	7
Deficit	55	12	5
	£119	7	0

Liabilities.	£	s.	d.
By Messrs. Macmillan's Account for publishing "Brain"	119	7	0
	£119	7	0

Audited and found correct, December 20, 1901, { Leonard Guthrie, Purves Stewart.

Charles E. Beevor, *Hon. Treasurer.*

RULES.

1.—The Society shall be called the NEUROLOGICAL SOCIETY OF LONDON.

2.—The objects of the Society shall be to promote the advance of Neurology and to facilitate intercourse amongst those who cultivate it, whether from a Psychological, Physiological, Anatomical, or Pathological point of view.

3.—The Society shall consist of Ordinary, Corresponding, and Honorary Members.

4.—Any one engaged in researches bearing on Neurology, or manifesting interest in such researches, shall be eligible for the Ordinary Membership.

5.—Men of distinction in Science, who have contributed to the advancement of Neurology, shall be eligible for the Honorary, or for the Corresponding Membership.

6.—The number of Honorary Members shall be limited to six, and that of Corresponding Members to twelve.

7.—Honorary and Corresponding Members shall have the right of attending the Meetings of the Society and of taking part in them.

8.—Honorary and Corresponding Members shall be elected by the Society on the recommendation of the Council

9.—Candidates for Ordinary Membership shall be recommended by at least three Members of the Society, who shall append their names to a printed form supplied by the Secretaries to any person seeking Membership.

10.—The Council shall nominate candidates for election into the Society as Ordinary Members from among persons so recommended.

11.—The names of Candidates nominated by the Council shall be submitted to the next Meeting of the Society, and shall be balloted for at the next subsequent meeting, one black ball in ten excluding.

12.—The Annual Subscription of an Ordinary Member shall be One Guinea, due in advance.

13.—The Treasurer shall send to each Member, shortly before the Annual General Meeting, a notice reminding him that his Subscription becomes due on that day.

14.—Non-payment of the Subscription within twelve months after it is due, shall be considered as equivalent to resignation.

15.—The Council shall consist of a President, two Vice-Presidents, two Secretaries, one Treasurer, and ten Councillors.

16.—Five Members of the Council shall form a quorum.

17.—The office of President shall be tenable for one year, and be entered upon at the beginning of each year by the Senior Vice-President.

18.—The office of Vice-President shall be tenable for two years, one Vice-President being elected every year.

19.—The Secretaries and Treasurer shall be elected annually with eligibility for re-election.

20.—The Councillors shall be elected for one year, and not more than eight shall be eligible for re-election to the same office during the following year.

21.—One full week before the Annual General Meeting, the Secretaries shall send to each Member a balloting paper containing the names of the Officers and Councillors whom the Council nominate for the ensuing year.

22.—The Society shall elect the Council by ballot, each Member, however, being at liberty to substitute other names for any of those upon the list.

23.—There shall be six Ordinary Meetings annually, of which the first held in each year shall be the Annual General Meeting.

24.—Notices of each meeting, and of the subjects to be considered, shall be sent by the Secretaries to each Member of the Society at least one week before the meeting.

25.—Special Meetings shall be held at the option of the Council, or at the request, in writing, of twenty Members.

26.—The President shall have the power of inviting any person to attend and to take part in the scientific work of the meeting.

27.—If at any time the Council shall be of opinion that the interests of the Society require the expulsion of a Member, they shall submit the question to a special General Meeting, at which, if more than one-half of the Members of the Society vote, by ballot as usual, for the expulsion of the Member, his subscription for the current year shall be returned to him, and he shall thereupon cease to be a Member of the Society.

28.—The Council shall draw up and submit for the approval of the Society, supplementary rules regulating the dates, places, and character of the meetings; shall propose special subjects for investigation by the Society, and shall nominate sub-committees for the methodical carrying out of such investigations. They shall decide, from time to time, on the form of publication which its proceedings are to assume.

29.—No alteration shall be made in the present rules, excepting at the Annual Meeting, or at a Special Meeting convened for the purpose, and unless it be proposed by the Council, or in writing by at least twenty Members, the usual notice be given of the proposed change to every Member before the meeting at which it is to be brought forward.

Each Member receives quarterly, from the beginning of the year in which he is elected, a copy of "BRAIN; a Journal of Neurology," the organ of the Society, and edited for it by R. Percy Smith, M.D., F.R.C.P.

HONORARY MEMBERS.

Mr. Herbert Spencer, London.
Professor Wundt, Leipzig.
„ Hitzig, Halle.
Sir Samuel Wilks, Bart., London.

CORRESPONDING MEMBERS.

Professor Erb, Heidelberg.
„ Golgi, Pavia.
„ Goltz, Strasburg.
„ Grasset, Montpellier.
„ Jolly, Berlin.
„ Luciani, Rome.
„ Munk, Berlin.
„ Obersteiner, Vienna.
„ Retzius, Gustaf, Stockholm.
„ Ribot, Paris.
Dr. Weir Mitchell, Philadelphia.

LIST OF PRESIDENTS FROM THE FOUNDATION OF THE SOCIETY.

1886 J. Hughlings Jackson, M.D., F.R.S.
1887 Sir Samuel Wilks, Bart., M.D., F.R.S.
1888 Sir James Crichton-Browne, M.D., F.R.S.
1889 Jonathan Hutchinson, F.R.S.
1890 Thomas Buzzard, M.D.
1891 John S. Bristowe, M.D., F.R.S.
1892 H. Charlton Bastian, M.D., F.R.S.
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1894 David Ferrier, M.D., F.R.S.
1895 Sir William H. Broadbent, Bart., M.D., F.R.S.
1896 Alexander Hill, M.A., M.D.
1897 George H. Savage, M.D.
1898 Victor Horsley, M.B., F.R.C.S., F.R.S.
1899 W. H. Gaskell, M.D., F.R.S.
1900 Augustus Waller, M.D., F.R.S.
1901 W. Julius Mickle, M.D.
1902 Herbert William Page, M.A., F.R.S.

LIST OF HUGHLINGS JACKSON LECTURERS.

1897 J. Hughlings Jackson, M.D., F.R.S.
1900 Professor Eduard Hitzig, Halle.

*** Members are requested to communicate with the Secretaries when corrections are necessary.

—:o:—

EXPLANATION OF ABBREVIATIONS.

O.M., Original Member.	Tr., Treasurer.
Pres., President.	Sec., Secretary.
V.-P., Vice-President.	C., Member of Council.

H.J.L., Hughlings Jackson Lecturer.

ORDINARY MEMBERS.

Elected

1899 ABRAHAMS, BERTRAM, M.B., M.R.C.P., 14, Welbeck Street, W.

1892 ALEXANDER, ROBERT REID, M.D., The Asylum, Hanwell, W.

1897 ANDERSON, H. KERR, M.B., B.Sc., Whitefield, Great Shelford, Cambs.

1894 ANDRIEZEN, W. LLOYD, M.D., 7, Apsley Terrace, Acton, W.

1891 BALLANCE, C. A., M.S., F.R.C.S., 106, Harley Street, W. (C., 1897-1900.)

O.M. BARLOW, Sir THOMAS, Bart., M.D., F.R.C.P., 10, Wimpole Street, W.

1897 BARRATT, J. O. WAKELIN, M.D., F.R.C.S., Pathological Laboratory, West Riding Asylum, Wakefield.

O.M. BASTIAN, H. CHARLTON, M.D., F.R.C.P., F.R.S., 8A, Manchester Square, W. (Pres., 1892; V.-P., 1891; C., 1886-89, 1893-95.)

1897 BATTEN, FREDERICK E., M.D., F.R.C.P., 33, Harley Street, W.

O.M. BEACH, FLETCHER, M.B., F.R.C.P., Winchester House, Kingston Hill, Surrey.

,, BEEVOR, C. E., M.D., F.R.C.P., 135, Harley Street, W. (Tr., 1894-1902; C., 1893.)

1888 BIRT, ERNEST, M.D., West Riding Asylum, Wakefield.

1898 BOLTON, JOSEPH SHAW, M.D., B.S., B.Sc., Claybury Hall, Woodford, Essex.

1896 BOND, C. HUBERT, M.D., D.Sc., London County Asylum, Bexley, Kent.

1899 BOND, J. W., M.D., B.S., 26, Harley Street, W.

1892 BOWLBY, ANTHONY A., F.R.C.S., 24, Manchester Square, W.

1898 BOYCE, RUPERT W., M.B., University College, Liverpool.

,, BRADBURY, JOHN B., M.D., F.R.C.P., 4, St. Peter's Terrace, Cambridge.

1889 BRADFORD, J. R., M.D., D.Sc., F.R.C.P., F.R.S., 8, Manchester Square, W.

O.M. BRAMWELL, BYROM, M.D., F.R.C.P.Ed., 23, Drumsheugh Gardens, Edinburgh. (C., 1894.)

1899 BRAMWELL, EDWIN, M.B., C.M., M.R.C.P., 2, Randolph Place, Edinburgh.

1895 BRAMWELL, JOHN MILNE, M.B., C.M., 15, Stratford Place, W.

1892 BRISTOWE, HUBERT CARPENTER, M.D., Wrington, Somerset.

Elected

O.M. BROADBENT, Sir WM. H., Bart., M.D., F.R.C.P., F.R.S., 84, Brook Street, W. (Pres., 1895; V.-P., 1893; C., 1886-87, 1896.)

1894 BRODIE, T. GREGOR, M.D., 55, Marlborough Mansions, West Hampstead, N.W.

1897 BROWN, H. H., M.D., F.R.C.S., 22, Museum Street, Ipswich.

1888 BROWN, SANGER, M.D., 100, State Street, Chicago.

O.M. BRUCE, ALEX., M.D., F.R.C.P.Ed., 8, Ainslie Place, Edinburgh. (C., 1895.)

,, BRUCE, J. MITCHELL, M.D., F.R.C.P., 23, Harley Street, W.

1898 BRUCE, SAMUEL NOBLE, M.R.C.S., 15, Queensboro' Terrace, Hyde Park, W.

O.M. BRUNTON, Sir T. LAUDER, M.D., F.R.C.P., F.R.S., 10, Stratford Place, W. (C., 1896-98.)

1895 BRYAN, FREDERICK, M.B., Horton Manor Asylum, Banstead Downs, Surrey.

,, BRYANT, JOHN HENRY, M.D., F.R.C.P., 8, Mansfield Street, Portland Place, W.

1890 BURY, JUDSON SYKES, M.D., F.R.C.P., 10, St. John Street, Manchester.

1900 BUZZARD, E. FARQUHAR, M.B., M.R.C.P., 33, Harley Street, W.

O.M. BUZZARD, THOMAS, M.D., F.R.C.P., 74, Grosvenor Street, W. (Pres., 1890; V.-P., 1888-89; C., 1886-87, 1891-95.)

1898 CALEY, H. A., M.D., F.R.C.P., 24, Upper Berkeley Street, W.

,, CAMPBELL, HARRY, M.D., F.R.C.P., 23, Wimpole Street, W.

1887 CATTELL, J. MCK., M.A., Ph.D., Columbia College, New York, U.S.A.

1899 CHAMBERS, JAMES, M.A., M.D., The Priory, Roehampton.

1891 CLARKE, J. MICHELL, M.D., F.R.C.P., 28, Pembroke Road, Clifton, Bristol.

1892 COLE, ROBERT HENRY, M.D., M.R.C.P., 48, Upper Berkeley Street, Portman Square.

1899 COLLIER, J. S., M.D., B.Sc., M.R.C.P., 57A, Wimpole Street, W.

1890 COLMAN, W. S., M.D., F.R.C.P., 22, Wimpole Street, W. (Sec., 1899-1902.)

,, CORNER, HARRY, M.D., Brook House, Southgate, Middlesex.

1899 COUPLAND, SIDNEY, M.D., F.R.C.P., 16, Queen Anne Street, W.

1901 COX, JOSHUA JOHN, M.D., St. Ronan's, Clarendon Road, Eccles, Manchester.

1901 CRAIG, MAURICE, M.D., M.R.C.P., Bethlehem Royal Hospital, S.E.

1895 DAVIDSON, ANDREW, M.D., The County Asylum, Dorchester, Dorset.

1897 DAWSON, WILLIAM R., M.D., F.R.C.P.I., Farnham House, Finglas, Co. Dublin, Ireland.

1894 DEAN, H. PERCY, M.S., F.R.C.S., 69, Harley Street, W.

1898 DODD, HENRY WORK, F.R.C.S., 136, Harley Street, W.

O.M. DRESCHFELD, JULIUS, M.D., F.R.C.P., 3, St. Peter's Square, Manchester. (V.-P., 1898-99.)

,, DRUMMOND, DAVID, M.D., 6, Saville Place, Newcastle-on-Tyne.

1892 DUPUY, EUGENE, M.D., 53, Avenue Montaigne, Paris.

Elected

1901 EDRIDGE-GREEN, F. W., M.D., F.R.C.S., Hendon Grove, Hendon, N.W.

1899 FAWCETT, JOHN, M.D., M.R.C.P., 26, St. Thomas Street, S.E.

O.M. FERRIER, DAVID, M.D., F.R.C.P., F.R.S., 34, Cavendish Square, W. (Pres., 1886; V.-P., 1892-3; C., 1886-90-95.)

,, GASKELL, W. H., M.D., F.R.S., The Uplands, Great Shelford, Cambs. (Pres., 1899; V.-P., 1897-98; C., 1896, 1900.)

,, GEE, SAMUEL J., M.D., F.R.C.P., 31, Upper Brook Street, W.

,, GODLEE, R. J., M.B., F.R.C.S., 19, Wimpole Street, W.

1899 GOODALL, EDWIN, M.D., M.R.C.P., Joint Counties Asylum, Carmarthen.

1898 GOODLIFFE, JNO. HENRY, M.D. Aberd., 802, High Road, Lower Tottenham.

1897 GOSSAGE, ALFRED MILNE, M.B., M.R.C.P., 54, Upper Berkeley Street, W.

1892 GOTCH, FRANCIS, M.A., F.R.S., The Lawn, Banbury Road, Oxford.

1893 GRANT, J. DUNDAS, M.D., F.R.C.S., 18, Cavendish Square, W.

O.M. GUNN, R. MARCUS, M.B., F.R.C.S., 54, Queen Anne Street, W. (C., 1899-1900.)

1895 GUTHRIE, LEONARD, M.D., F.R.C.P., 15, Upper Berkeley Street, W.

1901 HALL, W. HAMILTON, M.R.C.S., Fordcombe, Tunbridge Wells.

1893 HALLIBURTON, WILLIAM DOBINSON, M.D., F.R.C.P., F.R.S., Church Cottage, 17, Marylebone Road, N.W.

O.M. HAMILTON, D. J., M.B., F.R.S.E., University, Aberdeen.

1898 HANBURY, WILLIAM R., M.R.C.S., L.R.C.P., West Ham Borough Asylum, Goodmayes, Ilford.

1897 HARRIS, WILFRED J., M.D., M.R.C.P., 37, Queen Anne Street, W.

1898 HARTLEY, W. DARLEY, M.D., M.R.C.P., Park House, Kloof Street, Cape Town, South Africa.

,, HASLETT, JOHN HANFIELD, M.R.C.S., L.R.C.P., Halliford House, Sunbury-on-Thames.

1891 HAWKINS, HERBERT PENNELL, M.D., F.R.C.P., 56, Portland Place, W.

O.M. HAYCRAFT, J. B., M.D., D.Sc., F.R.S.E., 1, St. Andrew's Place, Cardiff.

1891 HEAD, HENRY, M.D., F.R.C.P., F.R.S., 61, Wimpole Street, W. (C., 1900; Sec., 1901-1902.)

O.M. HILL, ALEX., M.A., M.D., Downing Lodge, Cambridge. (Pres., 1896; V.-P., 1895; C., 1892-94.)

O.M. HORSLEY, VICTOR, F.R.C.S., F.R.S., 25, Cavendish Square, W. (Pres., 1898; V.-P., 1896-97; C., 1892-93, 1899.)

1889 HUGGARD, WILLIAM R., M.D., F.R.C.P., Davoz Platz, Switzerland.

1896 HULME, GEORGE FREDERICK, M.B., C.M., South View, Montague Road, Felixstowe.

1889 HUMPHRY, LAURENCE, M.D., M.R.C.P., Lensfield, Cambridge.

1901 HUNTER, WILLIAM, M.B., C.M., London Hospital Medical College, E.

O.M. HUTCHINSON, JONATHAN, F.R.C.S., F.R.S., 15, Cavendish Square, W. (Pres., 1889; V.-P., 1887-88; C., 1886, 1890.)

1889 HYSLOP, T. B., M.D., C.M., Bethlem Royal Hospital, Lambeth, S.E.

Elected

O.M. JACKSON, J. HUGHLINGS, M.D., F.R.C.P., F.R.S., 3, Manchester Square, W. (Pres., 1886; H.J.L., 1897; C., 1887, 1892.)

,, JESSOP, W. H., M.B., F.R.C.S., 73, Harley Street, W.

1895 JOHNSTON, GEORGE, M.D., M.R.C.P., 3, Montagu Place, Montagu Square, W.

1892 JONES, HENRY LEWIS, M.D., F.R.C.P., 61, Wimpole Street, W.

1894 JONES, ROBERT, M.D., F.R.C.S., Claybury Asylum, Woodford, Essex.

1901 KELYNACK, T. N., M.D., M.R.C.P., 53, Harley Street, W.

1894 KIDD, PERCY, M.D., F.R.C.P., 60, Brook Street, W.

1896 LANGDON, F. W., M.D., Cincinnati, Ohio, U.S.A.

1898 LANGDON-DOWN, REGINALD L., M.B., M.R.C.P., 47, Welbeck Street, W.

O.M. LANGLEY, J. N., M.A., D.Sc., F.R.S., Trinity College, Cambridge. (V.-P., 1901-1902; C., 1898-99.)

1888 LAWFORD, J. B., M.D., F.R.C.S., 99, Harley Street, W. (C., 1902.)

O.M. LEES, D. B., M.D., F.R.C.P., 22, Weymouth Street, W. (C., 1901-1902.)

1897 LEWIS, H. WOLSELEY, M.R.C.S., L.R.C.P., London County Asylum, Banstead, Surrey.

1901 LITTLE, E. GRAHAM, M.D., M.R.C.P., 61, Wimpole Street, W.

1897 LOEWENTHAL, MAX, M.D., M.R.C.P., 126, Princes' Road, Liverpool.

1899 LORD, JOHN R., M.B., C.M., London County Asylum, Bexley, Kent.

1898 MACCORMAC, JOHN M'GEE, M.D., 31, Victoria Place, Belfast.

,, MCALDOWIE, ALEXANDER M., M.D., 6, Brook Street, Stoke-on-Trent.

1891 MACDONALD, PETER WILLIAM, M.D., C.M., The County Asylum, Dorchester, Dorset.

,, MACKENZIE, HECTOR WILLIAM GAVIN, M.D., F.R.C.P., 34, Upper Brook Street, Grosvenor Square, W.

O.M. MACKENZIE, STEPHEN, M.D., F.R.C.P., 18, Cavendish Square, W. (C., 1896-98.)

1896 MACKINTOSH, ASHLEY W., M.A., M.D., 9, Bon Accord Square, Aberdeen.

1899 MACLULICH, PEERS, M.D., B.Ch., Joint Counties Asylum, Carmarthen.

1889 MACPHAIL, S. R., M.D., Borough Asylum, Rowditch, Derby.

O.M. MAGUIRE, ROBERT, M.D., F.R.C.P., 4, Seymour Street, W. (Sec., 1890-93; C., 1893-96.)

,, MANN, J. DIXON, M.D., F.R.C.P., 16, St. John's Street, Manchester.

,, MARRIS, W. A., M.D., The Vron, Ascot Road, Moseley, Birmingham.

1894 MARTIN, SIDNEY, M.D., F.R.C.P., F.R.S., 10, Mansfield Street, W.

1891 MAY, W. PAGE, M.D., M.R.C.P., Helouan, Cairo, Egypt.

1890 MENZIES, WILLIAM FRANCIS, M.D., B.Sc., M.R.C.P., Cheddleton Asylum, Leek, Staffordshire.

O.M. MERCIER, C., M.B., M.R.C.P., Flower House, Southend, Catford, S.E. (C., 1899-1902.)

Elected

1897 MEYER, ADOLF, M.D., Clark University, Worcester, Mass., U.S.A.

O.M. MICKLE, W. JULIUS, M.D., F.R.C.P., Grove Hall Asylum, Bow, E. (Pres., 1901; V.-P., 1900; C., 1895-97, 1902.)

1895 MOORE, NORMAN, M.D., F.R.C.P., 94, Gloucester Place, W.

O.M. MORRIS, MALCOLM, F.R.C.S.Ed., 8, Harley Street, W.

1888 MOTT, F. W., M.D., F.R.C.P., F.R.S., 25, Nottingham Place, W. (Sec., 1894-98; C., 1899-1902.)

1899 MOULD, GILBERT E., M.R.C.S., L.R.C.P., The Grange, nr. Rotherham,

1901 MOULD, GEORGE WM., M.R.C.S., Cheadle Royal Asylum, Manchester.

1894 MURRAY, GEORGE R., M.A., M.D., F.R.C.P., 11, Ellison Place, Newcastle-on-Tyne.

1889 MURRAY, H. MONTAGUE, M.D., F.R.C.P., 25, Manchester Square, W.

O.M. NETTLESHIP, EDWARD, F.R.C.S., Shottermill, Haslemere, Surrey.

,, NICOLSON, DAVID, C.B., M.D., M.R.C.P.Ed., Balgownie, Guildford, Surrey.

1888 NIERMEYER, J. H. H., M.D., Amsterdam.

,, NORMAN, CONOLLY, F.R.C.P.I., F.R.C.S.I., St. Dymphna's, N. Circular Road, Dublin.

1887 OGILVIE, GEORGE, M.B., M.R.C.P., 22, Welbeck Street, W.

,, OLIVER, THOMAS, M.D., F.R.C.P., 7, Ellison Place, Newcastle-on-Tyne,

O.M. ORANGE, WM., C.B., M.D., F.R.C.P., The Bryn, Godalming, Surrey.

,, ORD, W. M., M.D., F.R.C.P., Hurstbourne Tarrant, Andover. (C., 1893-94.)

,, ORMEROD, J. A., M.D., F.R.C.P., 25, Upper Wimpole Street, W. (C., 1895-97.)

,, ORR, DAVID, M.B., County Asylum, Prestwich, Manchester.

,, PAGE, HERBERT WILLIAM, M.A., F.R.C.S., 146, Harley Street, W. (Pres., 1902; V.-P., 1900-1; C., 1891-92.)

1895 PARKINSON, JOHN PORTER, M.D., M.R.C.P., 57, Wimpole Street, W.

1901 PARSONS, JOHN HERBERT, M.B., B.Sc., 28, Great Ormond Street, W.C.

1901 PASSMORE, E. S., M.D., M.R.C.P., Banstead Downs, Sutton, Surrey.

1896 PATERSON, DONALD ROSE, M.D., M.R.C.P., 15, St. Andrew's Crescent, Cardiff.

1895 PINDER, GEORGE, M.D., St. Swithin's, Worthing.

1899 PIPER, FRANCIS P., M.B., M.R.C.S., L.R.C.P., Claybury Asylum, Woodford, Essex.

1888 PITT, G. N., M.D., F.R.C.P., 15, Portland Place, W.

O.M. POORE, G. VIVIAN, M.D., F.R.C.P., 24A, Portland Place, W. (C., 1898-99.)

,, PURVES, W. LAIDLAW, M.D., 20, Stratford Place, W.

1899 RAMBAUT, DANIEL F., M.D., B.Ch., Richmond District Asylum, Dublin.

1894 RANSOM, WILLIAM B., M.D., F.R.C.P., The Pavement, Nottingham.

Elected

1890 RAYNER, HENRY, M.D., M.R.C.P.Ed., 16, Queen Anne Street, W.

O.M. REID, E. W., M.B., F.R.S., University College, Dundee.

1897 REISSMANN, CHARLES H., M.B., B.Sc., Knutsford, Glenelg, South Australia.

1893 RENNIE, GEORGE E., M.D., M.R.C.P., College Street, Sydney.

1895 REYNOLDS, ERNEST S., M.D., F.R.C.P., 2, St. Peter's Square, Manchester.

1892 RICHARDS, JOSEPH PEEKE, M.R.C.S., 6, Freeland Road, Ealing, W.

1891 RIVERS, W. H. R., M.A., M.D., F.R.C.P., St. John's College, Cambridge. (C., 1897-98.)

1898 ROBERTSON, WILLIAM FORD, M.D., 7, Hill Square, Edinburgh.

1892 ROWE, EDMUND LEWIS, L.R.C.P., L.R.C.S., Borough Asylum, Ipswich.

1901 ROWS, R. G., M.D., County Asylum, Whittingham, Manchester.

1892 RUFFER, MARC ARMAND, M.D., Alexandria, Egypt.

1889 RUSSELL, J. S. RISIEN, M.D., F.R.C.P., 44, Wimpole Street, W. (Sec., 1896-1900; C., 1901-1902.)

1899 RUSSELL, J. W., M.D., M.R.C.P., 72, Newhall Street, Birmingham.

1901 SALAMAN, REDCLIFFE N., M.A., M.B., Wentworth House, Mill Hill, N.W.

O.M. SANDERSON, Sir J. BURDON, Bart., M.D., F.R.C.P., F.R.S., Banbury Road, Oxford.

,, SAVAGE, G. H., M.D., F.R.C.P., 3, Henrietta Street, Cavendish Square. (Pres., 1897; V.-P., 1895; C., 1886-90, 1898.)

1888 SAVILL, T. D., M.D., M.R.C.P., 60, Upper Berkeley Street, W.

O.M. SCHÄFER, E. A., F.R.S., University of Edinburgh. (Pres., 1893; V.-P., 1892; C., 1886-98.)

1901 SCHORSTEIN, GUSTAVE, M.D., F.R.C.P., 11, Portland Place, W.

O.M. SEMON, Sir FELIX, M.D., F.R.C.P., 39, Wimpole Street, W. (C., 1899-1901.)

1898 SEWARD, WM. JOSEPH, M.B., Colney Hatch Asylum, N.

O.M. SHARKEY, S. J., M.D., F.R.C.P., 22, Harley Street, W. (V.-P., 1902; C., 1899-92.)

,, SHERRINGTON, C. S., M.D., F.R.S., 16, Grove Park, Liverpool. (C., 1892-95.)

1894 SHUTTLEWORTH, GEORGE E., M.D., Ancaster House, Richmond.

1898 SIMPSON, FRANCIS O., L.R.C.P., M.R.C.S., Rainhill Asylum, Liverpool.

1900 SINGER, H. D., M.D., M.R.C.P., St. Thomas's Hospital, S.E.

1895 SMITH, F. J., M.D., F.R.C.P., 138, Harley Street, W.

1887 SMITH, R. PERCY, M.D., F.R.C.P., 36, Queen Anne Street, W. (Editor of "Brain," 1901-1902.)

1895 SPICER, W. T. HOLMES, M.D., F.R.C.S., 5, Wimpole Street, W.

1901 STAFFORD, WILLIAM, M.B., 110, Mansfield Road, Nottingham.

1895 STANSFIELD, THOS. E. K., M.B., London County Asylum, Bexley, Kent.

1895 STANLEY, DOUGLAS, M.D., 19, Easy Row, Birmingham.

1892 STARLING, ERNEST HENRY, M.D., F.R.C.P., F.R.S., 8, Park Square, N.W.

1901 STEELL, GRAHAM, M.D., F.R.C.P., 96, Mosley Street, Manchester.

1897 STEWART, PURVES, M.A., M.D., M.R.C.P., 133, Harley Street, W.

Elected

1897 STIRLING, WM., M.D., D.Sc., Owens College, Manchester.
1894 STODART-WALKER, A., M.B., F.R.C.P.Ed., 30, Walker St., Edinburgh.
1897 STODDART, WM. H., M.D., M.R.C.P., Bethlem Royal Hospital, Lambeth, S.E.
1895 STOUT, G. F., M.A., 137, Woodstock Road, Oxford.
1887 SUCKLING, C. W., M.D., M.R.C.P., 103, Newhall Street, Birmingham.
1888 SYERS, HENRY W., M.D., M.R.C.P., 75, Wimpole Street, W.

1898 TAYLOR, F. R. P., M.D., Darenth Asylums and Schools, Dartford, Kent.
1891 TAYLOR, JAMES, M.D., F.R.C.P., 49, Welbeck Street, W. (C., 1900-2.)
1895 TELFORD-SMITH, T., M.A., M.D., Romansleigh, Wimborne, Dorset.
1898 THOMSON, H. CAMPBELL, M.D., M.R.C.P., 34, Queen Anne Street, W.
1889 THORBURN, WM., F.R.C.S., The Limes, Nelson Street, Manchester. (C., 1901-1902.)
1892 TITCHENER, E. B., B.A., Ph.D., 72, Heustis Street, Ithaca, N.Y.
O.M. TOOTH, H. H., M.D., F.R.C.P., 34, Harley Street, W. (Sec., 1891-95; C., 1896-99.)
1892 TREVELYAN, E. F., M.D., B.Sc., F.R.C.P., 40, Park Square, Leeds.
,, TUCKEY, CHARLES LLOYD, M.D., 88, Park Street, Grosvenor Square, W.
,, TUKE, Sir J. BATTY, M.D., F.R.C.P.Ed., 20, Charlotte Sq., Edinburgh.
1891 TUKE, THOMAS SEYMOUR, M.B., Chiswick House, Chiswick.
,, TURNER, WILLIAM ALDREN, M.D., F.R.C.P., 13, Queen Anne Street, W.
1898 TURNEY, HORACE G., M.D., F.R.C.P., 68, Portland Place, W.
O.M. TWEEDY, JOHN, F.R.C.S., 100, Harley Street, W.

1901 VINCENT, SWALE, M.B., 137, Richmond Road, Cardiff.
1888 VOORTHUS, J. A., M.D., Apeldoorn, 542, Loulaan, Netherlands.

O.M. WALLER, AUGUSTUS, M.D., F.R.S., 16, Grove End Road, N.W. (Pres., 1900; V.-P., 1899; C., 1894-97, 1901.)
,, WARD, J., D.Sc., Trinity College, Cambridge.
,, WARNER, FRANCIS, M.D., F.R.C.P., 5, Prince of Wales Terrace, Kensington Palace, W.
1901 WARRINGTON, W. B., M.D., M.R.C.P., 69, Rodney Street, Liverpool.
1892 WASHBOURN, J. W., M.D., F.R.C.P., 6, Cavendish Place, W.
O.M. WATTEVILLE, A. DE, M.A., M.B., B.Sc., 30, Welbeck Street, W. (C., 1890-95, 1896-1902; Sec., 1886-89; Editor of "Brain," 1880-1900.)
1897 WEBER, F. PARKES, M.D., F.R.C.P., 19, Harley Street, W.
,, WEST, SAMUEL, M.D., F.R.C.P., 15, Wimpole Street, W.
1897 WHITE, ERNEST W., M.B., M.R.C.P., City of London Asylum, Dartford.
O.M. WHITE, W. HALE, M.D., F.R.C.P., 65, Harley St., W. (C., 1897-1902.)
1894 WHITING, ARTHUR J., M.D., M.R.C.P., 142, Harley Street, W.
1889 WIGLESWORTH, JOSEPH, M.D., F.R.C.P., County Asylum, Rainhill, Lancashire.

Elected

1900 WILLIAMS, LEONARD, M.D., 8, York Street, Portman Square, W.

1894 WILLIAMSON, RICHARD T., M.D., F.R.C.P., 294, Oxford Road, Manchester.

1896 WILSON, ALBERT, M.D., M.R.C.P., Minto House, South Woodford, Essex.

,, WOOD, GUY M., M.B., M.R.C.P., 6, Woburn Square, W.C.

1889 WOOD, T. OUTTERSON, M.D., M.R.C.P., 40, Margaret Street, Cavendish Square, W.

1892 WOODHEAD, G. SIMS, M.D., F.R.C.P.Ed., 6, Scrope Terrace, Cambridge.

1899 WRIGHT, HAMILTON, M.D., Pathological Institute, Selangor Straits Settlement.

1898 YOUNG, ROBERT ARTHUR, M.D., B.Sc., M.R.C.P., 41, Wimpole St., W.